Clinical Profile of Children With Extra Cranial Germ Cell Tumors

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A DISSERTATION SUBMITTED TO THE
TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY,
IN PARTIAL FULFILLMENT OF THE REQUIREMENT
FOR THE
MCh. PAEDIATRIC SURGERY EXAMINATION
TO BE HELD IN AUGUST 2014

Certificate

This is to certify that the dissertation entitled

Clinical Profile of Children with Extra Cranial Germ Cell Tumors

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In partial fulfillment of the

Tamil Nadu Dr. M.G.R. Medical University, rules and regulations,

For the award of the degree of **MCh. Paediatric Surgery**

Under my guidance and supervision during the academic year **2014**

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ABSTRACT

Title: **Clinical Profile of Children with Extra Cranial Germ Cell Tumors**

Aim/Objectives:

To assess the clinico-pathological profile and the long term effects of treatment in children, with extracranial germ cell tumors (GCTs).

Materials and Methods:

All children below the age of 16 years who presented to the department of Paediatric Surgery with GCTs between January 2003 and December 2012 were included in this study. This was a retrospective study looking at the patient data base. All eligible patients were informed by mail and phone by the investigator and requested to attend the outpatient department for follow up. Data was analyzed using descriptive statistical methods for continuous and categorical variables. Binary logistic regression was used to look at risk factors, and Kaplan Meier curves for overall survival and event free survival.

Results:

107 children with GCTs were studied for the period between 2003 to 2012, 64% were female and 36% were male, 56% were below 5 years of age. A majority were found to have ovarian GCTs (28%) followed by sacrococcygeal (23%) and testicular (15%) tumors. Malignancy was found in 46%, the commonest being yolk sac tumor. Elevated Alpha feto protein was found in all children with malignancy. Surgery alone or in combination with chemotherapy was used to treat

these tumors. Overall survival and event free survival for malignant GCTs was 85.2% and 75.9% respectively. Median survival was 44 months.

Conclusions:

GCTs are rare tumors which occur at many different sites. They are more common in females and have different age peaks for different sites. Non gonadal sites predominate in early childhood, while gonadal GCTs are more common during the later part of childhood and adolescence. Benign tumors are more common. Malignancy can occur, with Yolk Sac tumors being the commonest. Multimodality treatment with surgery and chemotherapy has excellent results in malignant tumors. Long term follow up is advisable for all patients who have GCTs.

Key Words: Extra Cranial Germ Cell Tumors, Children, Clinical Profile, Outcomes

ACKNOWLEDGEMENTS

I am grateful to God almighty for an opportunity to study a subject which has been close to my heart.

To Dr Sampath Karl, my guide and mentor, for his extreme patience, and care in going through this thesis and giving it direction.

To Dr Sudipta Sen, a great teacher, for his encouragement at different points of this study.

To Dr John Mathai, and Dr Reju Thomas for their valuable suggestions.

To Dr Leni Mathew and her colleagues for their help with patients and their data

To my colleagues Dr Susan Jehangir, Dr Pradeep Ninan, Dr Harshjit Singh Bal, Dr Sundeep Kisku and Ravi Kishore for their inputs, and making complicated things look simple

To Dr Ramani Kumar for helping with the histopathology pictures

To my peers for their camaraderie

To Mrs. Grace Rebecca, for her help with the analysis.

To my wife Ashita, who has so lovingly supported me, through this time, and kept me from giving up.

To my children Arnav and Tara for putting up with a lot through it all

To my parents and in laws who have supported this venture with full enthusiasm and prayer and

And last but not least, to all the children who suffer from these tumors, hope this work will help them in some way.

TABLE OF CONTENTS

INTRODUCTION

Germ cell tumors (GCTs) are a rare group of benign and malignant tumors which can occur at many different sites. These can be both gonadal and extragonadal. They occur in the para-axial locations like sacrococcygeal area, gonads, retroperitoneum, mediastinum, neck and pineal gland in order of frequency, due to the arrest or abnormal migration of primitive germ cells.

These tumors represent about 1-3% of all childhood tumors, and about 8-10% of all paediatric solid tumors. There is large spectrum of these tumors from the mature teratoma to the highly malignant embryonal carcinoma. Benign teratomas are the commonest although upto 30% malignancy has been described in various series.

Tumors of the extragonadal sites are the commonest during infancy and early childhood, and gonadal sites predominate during later childhood and adolescence. A bimodal peak has been described in various studies, but others have found a varying age peak for different sites. These tumors are commoner in females.

With the advent of highly sophisticated imaging like Magnetic resonance imaging (MRI) and Computed Tomography (CT) scan and tumor markers like Alpha feto protein (AFP) and Human chorionic gonadotropin (βHCG), the pick-up rate of malignancy has increased and these tumors now can be treated with proper diagnosis.

Surgery alone is used for benign tumors. A combination of surgery and chemotherapy (both preoperative and postoperative) is used to treat malignant tumors.

In the pre-chemotherapy era, survival of patients with malignancy treated with surgery alone was rare. Some progress was made in the initial days where Vincristine, Actinomycin D and Cyclophosphamide (VAC) was used. Platinum based chemotherapy protocols in the 1980s and 1990s using Cisplatinum, Bleomycin and Etoposide (PEB) or Carboplatin, Bleomycin, and Etoposide (JEB) are currently used as first line therapy and have improved survival immensely. Survival rates of almost 100% are recorded for children with low stage malignant gonadal GCTs. Survival rates of almost 90%-95% have been achieved with high stage gonadal GCTs. For the malignant extragonadal sites survival rates of 70-90% have been reported.

We present the clinical profile of 107 patients between January 2003 and December 2012 who presented to the department of paediatric surgery with extracranial germ cell tumors.

AIMS AND OBJECTIVES

1. To assess the clinico-pathological profile of patients who have presented to the department of Paediatric Surgery with Extracranial Germ Cell Tumors

2. To assess the long term effects of treatment (Surgery and Chemotherapy) in children with Extracranial Germ Cell Tumors

REVIEW OF LITERATURE

Germ cell tumors (GCT's) are tumors which arise from primitive germ cells. These are rare tumors which can occur anywhere in the body from the pineal gland to the genitourinary system. These tumors have a broad spectrum from the aggressive embryonal carcinoma to the benign mature teratoma. GCTs tend to occur in the midline or the para-axial locations of the body. This supports the theories of germ cell migration. Sacrococcygeal tumors are the most common, followed by gonadal, mediastinal, retroperitoneal and other rarer sites like the jaw, neck, vagina, and bladder.[1]

At a gestational age of four weeks germ cells arise from the yolk sac endoderm of the fetus. At about the sixth week they reach the genital ridge via the dorsal mesentry. This migration is determined by c-kit receptors and stem cell factors. If the migration of these germ cells is halted or is along an different path, germ cells get deposited in these areas and can form tumors anywhere mainly in the sacrococcygeal area.[2]

Incidence and epidemiology

Several studies have analyzed GCTs reporting an incidence between 0.3%-3% among all paediatric malignancies, and 8-10% for all paediatric solid tumors. There is a female preponderance with female to male ratio of 4-1.7:1. A higher incidence in females is thought to be due to higher number of ovarian tumors than testicular tumors. There is no predilection described to a specific geographic region or race.[1–8]

Embryology

Several theories have been proposed to explain the origin and location of these tumors. Some investigators support the theory of migration of primitive germ cells along an altered path. Another theory proposes that the totipotent cells which originate in the primitive knot and primitive streak give rise to these tumors, which invaginate between the layers of the bilaminar disc to form the mesoderm.[9]

Histology

There is a broad spectrum of histologic types which are classified as follows. Teratomas, which can be either mature or immature, germinomas arise in the ovary, and their counterparts, seminomas arise in the testes. The endodermal sinus tumor or yolk sac tumor, choriocarcinoma and embryonal carcinoma are also part of this spectrum.[1]

Telium proposed a holistic concept, a theory which speaks of germ cell tumors arising from totipotent primitive germ cells. These cells follow embryonic or extraembryonic differentiation. The tumors which follow extraembryonic differentiation are yolk sac tumors and choriocarcinoma. Yolk sac tumors secrete alfa fetoprotein (AFP) and choriocarcinoma, beta human chorionic gonadotropin (βHCG) respectively. Immature totipotent cells give rise to embryonal carcinoma. Teratomas are tumors which mimics organ structures of all germ layers in differentiation. The grade of immaturity is decided by the presence of neuroepithelial elements. Seminomas in males and dysgerminoma in females are tumors which represent undifferentiated germ epithelium. In contrast to adult germ cell tumors paediatric germ cell tumors do not develop from intratubular carcinoma in situ.[5]

Tumor Markers

A common histology in malignant GCTs is yolk sac tumors or endodermal sinus tumor. They secrete alfa fetoprotein (AFP). AFP should be estimated at the time of presentation. Human chorionic gonadotropin (βHCG) is produced by choriocarcinoma. These tumors are rarer than yolk sac tumors. Persistently elevated levels of these markers or rising levels after initial decline suggests non responsive or recurrent tumors.[4]

The human yolk sac produces alpha-fetoprotein (AFP), albumin, prealbumin, alpha-l-antitrypsin and transferrin. This was studied in cultured cells and nude mice which had transplanted tumor cells. Some proteins like alpha-fetoprotein and alpha-I-antitrypsin were synthesized by these cells. The production was studied in children with yolk sac tumor. Abnormally high levels of AFP were found in all these children. The other proteins were at normal levels. This can be explained by the fact that proteins other than AFP are present in large quantities in sera of normal people. AFP is seen only in small quantities in normal people. AFP can be correlated to the diagnosis and response to treatment for children with Yolk sac tumor. When the tumor is completely excised serum AFP reaches normal levels (0IU/ml) with a half-life of 4 days. In cases where only radiotherapy and chemotherapy has been used these remain elevated.[10]

Genetics

Malignant GCT tend to occur more in children with disorders of sexual differentiation(DSD), undescended testes, and Klinefelter's syndrome associated with thoracic teratomas. Children with DSD have and increased risk of developing gonadoblastoma. Gonadoblastoma can undergo transformation to yolk sac tumor, dygerminoma, immature teratoma or choriocarcinoma.[4]

Chromosomal abnormalities have been found in children who have malignant germ cell tumors. Children with benign tumors who are less than 4 years old have normal chromosomes. A majority of children with malignant GCTs from both gonadal and extra gonadal sites have abnormalities of chromosome 3. Girls with malignant ovarian GCTs had loss of 1p/gain of 1q. Among the boys with extragonadal GCTs, many have abnormalities of chromosome 21 and X chromosomes. Many have been found to have trisomy 21 and Klinefelter's syndrome. Many chromosomal anomalies are seen in children with testicular GCTs. These include near-triploidy, loss of chromosomes 11, 13, and 18, and gain of chromosomes 7, 8, the X chromosome, and an isochromosome 12p. In children with malignant GCTs deletion of 1p/gain of 1q and +3 are commonly seen.[11]

Age Distribution

A bimodal age distribution has been observed in germ cell tumors in some studies whereas others describe a different peak for different sites. There is a high incidence in early infancy and another peak seen after puberty. Majority of tumors diagnosed at birth are benign. Yolk sac tumor focus may be seen in a few. In early childhood yolk sac histology predominates. Seminomas and dygerminomas present after puberty. There is a high incidence of mixed GCTs in the form of embryonal carcinoma and choriocarcinoma. The incidence of GCT at non gonadal sites is high during infancy, whereas after puberty gonadal GCTs predominate. In childhood most non gonadal tumors are seen in females. After puberty a majority non gonadal tumors are seen in males.[1,3,5,12]

Imaging

A priority for diagnosis and management of germ cell tumors is good imaging. Imaging has been utilized in the initial diagnosis and also in the follow up of both benign and malignant germ cell tumors. With the advent of newer diagnostic modalities like the magnetic resonance imaging (MRI), and Positron emission Tomography (PET) the diagnosis, marking, treatment and follow up of these tumors has become easier.

It is now possible to detect teratomas, especially the ones located in the sacral region antenatally. Fetal MRI has now been used to confirm the diagnosis based on ultrasound evidence.(13) Sacrococcygeal teratomas are easy to diagnose once they present antenatally or in the neonatal period as most are evident on clinical examination. However the ones which present after the neonatal period should be evaluated by CT or MRI to mark out the extent of intrapelvic extension as this definitely has a role to play in the extent of surgery and the outcomes of patients.[14]

The use of thoracic and abdominal CT is considered a part of the protocol for children who are diagnosed to have testicular tumors. These scans delineate the retroperitoneal lymphnodes and can also be used to assess the possibility of metastasis in these. Lymph nodes which are greater than 2 cm are considered to be significant. CT is also used for follow up of such children as this can show the response to therapy.[15]

Tumors of the ovary present with abdominal pain or a mass. Some of these also present with acute abdomen. Most of these children will undergo an ultrasound examination. There is no specific radiology finding to differentiate between a malignant or benign mass. Therefore in addition to radiology tumor markers should also be evaluated to make a correct diagnosis.[16]

Imaging is very important in intra-abdominal and retroperitoneal tumors. These present with an abdominal mass or abdominal distention. Some of these may have reached a massive size before a doctor is consulted. It may be difficult to establish the site of origin of these masses even on ultrasound. Thus CT scan and MRI along with tumor markers are very important to establish diagnosis and the origin of such tumors.[2]

Mediastinal germ cell tumors are delineated by the use of highly advanced imaging like the MRI and CT scans. One can establish the site of origin and the related structures in the mediastinal germ cell tumors. Complete surgical extirpation may not be possible in mediastinal germ cell tumors and this can be evaluated on the imaging that is used. The follow up of the response to therapy can also seen on follow up imaging.[17]

The tumors of the miscellaneous sites can be evaluated by CT scan MRI or ultrasound. The extent, involvement of vital structures can be seen on CT scan. MRI has the advantage of being radiation free and better for soft tissue diagnosis.[18]

Classification

GCTs are commonly classified using the World Health Organization (WHO) classification. According to WHO GCTs are classified into 7 pathological types. These are dygerminoma, yolk sac tumor(endodermal sinus tumor), embryonal carcinoma, polyembryoma, choriocarcinoma, teratoma and gonadoblastoma. Dysgenetic gonads may give rise to gonadoblastoma, which is included in GCTs although it contains Sertoli cell components. [1,6,8]

Staging

There are various ways of staging GCTs. The Children's oncology group staging is one of them. The TNM classification has also been used. There is a system of risk stratification of germ cell tumors depending on age, stage, presence of immature elements, and distant metastasis. This system has also been developed by the children's oncology group (COG). Stage I is complete resection at any site including coccygectomy and negative tumor margins, stage II is microscopic residual disease, stage III is lymph node involvement with metastatic disease, gross residual disease, biopsy only, stage IV is distant metastasis including liver.[4]

Testicular tumors are staged a little differently as their pattern of spread is mainly through lymph nodes. Stage I is limited to testes, completely resected by high inguinal, orchiectomy, no clinical, radiological, or histological evidence of disease beyond the testis. Stage II is transcrotal orchiectomy or microscopic disease in the scrotum of high in the spermatic cord <5cm from proximal end, stage III is retroperitoneal lymphnode involvement but no visceral or extrabdominal involvement, lymph nodes >4cm by CT or >2cm and <4cm with biopsy proof, stage IV is distant metastasis including liver.[4]

Ovarian tumors have a different staging system. Stage I is limited to ovary, peritoneal evaluation is negative, Stage II is microscopic residual disease with no peritoneal involvement, Stage III is lymph node involvement with gross residual disease, and involvement of surrounding viscera, Stage IV is distant metastasis including liver.[4]

Risk Stratification

GCTs are now categorized into various risk strata to allow for more protocol based treatment.

Factors like age, site, type of histology, stage of tumor, whether the resection is complete and tumor markers like AFP and βHCG are used to stratify patients into risk groups in currently used treatment protocols. Such protocols have achieved a cure rate of over 80%. Low risk patients are now treated with a wait and watch policy or reduced chemotherapy. Patients who were previously thought to be high risk can have a favorable prognosis with treatment according to risk stratification.[19]

Low risk tumors are Stage I gonadal and all immature teratomas which require surgery and observation. Intermediate risk are Stage II-IV testis and Stage II-III ovary and stage I-II extragonadal which require surgery and 3 cycles of JEB chemotherapy, High risk tumors are Stage IV ovary and stage III –IV extragonadal tumors which require surgery and 4 cycles of chemotherapy.[4]

The French Society for Pediatric Oncology developed specific prognostic criteria for children with malignant GCT's. These included tumor markers, disease stage and primary site. The pediatric intergroup study found that age more than or equal to 12 years was the most important prognostic factor in children receiving platinum based chemotherapy.[8]

Treatment

Germ cell tumors can be benign or malignant. Those which are benign are treated with surgical excision alone. Multimodality therapy including chemotherapy, radiotherapy and surgery is used for malignant germ cell tumors. Chemotherapy can be used as neoadjuvant or preoperative chemotherapy, or post operative chemotherapy or both. Different tumor biology and histology cause these tumors to have variable response to chemotherapy and radiotherapy. Germinomatous

tumors respond well to both chemotherapy and radiotherapy. Non germinomatous tumors do not respond well to radiotherapy.[5]

Excellent outcomes have been seen in clinical trials done for management of extracranial malignant germ cell tumors (GCTs) in the western world. In developing countries like India the outcomes are different. A delay in presentation, misdiagnosis and abandonment of treatment are factors which contribute to poor results.[8]

Cisplatinum being introduced as a base for chemotherapy along with recent advances in surgery have improved results and prognosis in children with malignant GCTs. Adequate systemic tumor control is seen with platinum based chemotherapy. Recurrence may be seen if adequate local treatment is not given. Complete primary resection is possible in gonadal tumors, as these have a capsule which is well defined. Testicular GCTs are seen at a low stage of the disease. At sites where large tumors occur, like the sacrococcygeal and mediastinum, a primary resection may not be possible. After adequately evaluating these tumors, with tumor markers and imaging, preoperative chemotherapy can be given followed by surgery. Local and regional hyperthermia has been seen to enhance the effect of chemotherapy on tumor control. In tumors which do not secrete tumor markers a biopsy is mandatory.[19]

Several studies have been conducted in children to measure the effect of chemotherapy in advanced malignant germ cell tumors. Measurable disease remission has been seen in a majority of patients with regular chemotherapy protocols. There has been a dramatic improvement in survival and outcomes with the regimes followed now as compared to previously used regimes which included Methotrexate, Cytoxan and Dactinomycin.[19,20]

The MAKEI the MAHO trials used Cisplatinum, Etoposide and Bleomycin (PEB) for treatment whereas the UKCCSG GCII used Carboplatin, Bleomycin and Etoposide (JEB) for its study.

Carboplatin has less cumulative renal and ototoxicity which is seen with cispaltinum. The following are the dosage regimens used [5]

Drug	Dosage	Days
Cisplatinum	20mg/m^2	4,5,6,7,8
Bleomycin	15mg/m^2	1,2,3
Etoposide	80mg/m^2- 120mg/m^2	1,2,3
Carboplatin	600mg/m^2	1

Several other drugs like Ifosfamide 1800mg/m^2 and Vinblastine 1mg/m^2 have also been used in various other trials[5]. PEB and more commonly JEB are used in our institution.

Sacrococcygeal Teratoma (SCT)

Sacrococcygeal teratoma is the most frequently diagnosed germ cell tumor. An incidence of 1:25000 to1:35000 live births has been reported. According to literature it is predominantly seen in girls with a female to male ratio of 4:1. Three fourths of tumors present in the neonatal period, with most becoming evident by age 4 years.[1]

Altman and colleagues developed the classification of SCT in 1974. Type I tumors are almost entirely external, type II are primarily external with a small presacral component, type III are primarily presacral with a small external component, and type IV are entirely presacral. The overall risk of malignancy is 13% to 27%, but a strong correlation of malignancy with age at presentation is apparent. Benign tumors are seen in greater than 90% of children younger than age 2 months but present in less than half of children older than 2 months at presentation.[21]

The resection of sacrococcygeal teratomas follows the principles described by Gross et al in 1951.Complete removal of the tumor with excision of the coccyx, and resection which preserves the muscles and nerves are core. Some authors suggest early vascular control in tumors which are solid and very vascular. Some even suggest occlusion of the aorta, ligation of the internal iliac artery and the middle sacral artery in premature infants. Some authors suggest the surgery be performed in a supine position for good hemostasis and reducing respiratory compromise.

The muscle layers can be distorted by large tumors. It is very difficult to preserve and re-approximate these sphincter and gluteal muscles. Muscle stimulators can be very helpful at these times. The anal opening should also be placed properly in the perineum. Sometimes the anus can be placed posteriorly although within the sphincter. This poses problems in defecation. The skin closure is done in the Chevron fashion. A right angled flap has been described by Fishman et al which avoids scars below the gluteal crease and provides more tissue between the coccyx and anus.[1,4,22]

A retrospective study done at Tanta University and its associated hospitals, evaluated 35 patients with SCT, from 1998 to 2008. They found that children who presented as neonates had benign tumors with no recurrence in a follow up of 3-8 years. In children who presented beyond 6 months of age there was a high rate of recurrence.[14]

A study in Nigeria found SCT to occur more commonly in girls with 60.9% presenting immediately after birth and 85% of these tumors were found to be benign. There was recurrence in 4%. All malignant tumours had a significant presacral component. The benign tumors were resected. This study found 61% were type I, 24% type II, and 14% were type III.[22]

In a review of SCT Noteworthy et al found that 84% benign tumors. These benign tumors (mature and immature teratomas) presented externally (Altman type I) which helped in early

diagnosis and treatment. The immature tumors were larger than the mature teratomas and had malignant transformation in 16% patients. The malignant tumors like the embryonal and anaplastic carcinomas had a delayed age at diagnosis (average 21 months) and had a substantial presacral or endopelvic component (Altman types II–IV); this group had a bad prognosis with no survivors.[23]

Some studies have reported a high proportion of Altman type IV tumors. A majority of such patients present beyond the neonatal period. Good imaging is required to delineate the extent of these tumors which may include pelvic MRI. A large majority can be excised via the sacral route but a preliminary colostomy with abdominosacral excision may reduce morbidity in very large tumors.[24]

In a large study which followed up 117 patients with SCT, 25% were diagnosed prenatally, 63% at birth and 11% later in infancy. Resection was carried out via the sacral or abdominosacral route. 69% were mature teratomas, 20% were immature teratomas, and 11% were yolk sac tumors. Recurrence was seen in 2 patients with mature teratoma, and 7 with yolk sac tumor and 1 with immature teratoma. There was 33% recurrence seen in children with yolk sac tumor who were given no chemotherapy. The children were treated with adjuvant chemotherapy and had a 80% overall survival.[25]

Testicular GCTs

GCTs are rare in boys. They usually present as an enlarging testicular mass with or without associated hydrocoele. These children will need a scrotal ultrasound and tumor markers. A high orchidectomy is performed in boys with elevated tumor markers. This is followed by chemotherapy using the JEB protocol. Recurrence is assessed by tumor markers.[4]

Of the 34 testicular neoplasms in 33 boys studied by Abell and Holtz in 1963 over a 40 year period, 25 were germ cell tumors. All these boys were less than 12 years of age average being 17 months. Embryonal carcinoma was diagnosed in 14 of these children and benign teratoma in 10 children. One child had bilateral teratomas.[26]

Testicular GCTs have a familial predisposition in1-2% of cases. Brothers of children with testicular GCTs have a 8-10 fold risk, fathers have a 4-6 fold risk and twin brothers have a higher risk of developing tumors. The Y gr/gr deletion and mutations in PDE11A gene have increased risk of these tumors.[27]

The testis is the second most common site for yolk sac tumor. In one study of 37 patients with endodermal sinus tumor of different parts of the body, 10 had the tumor in the testis. All these patients were treated with a combination of chemotherapy and surgery. One patient had a retroperitoneal lymphadenectomy. All these patients were alive and well at follow up.[28]

In its consensus guidelines the European Germ Cell Cancer Consensus Group has recommended that primary surgery which can be a orchiectomy or organ preserving surgery along with monitoring of tumor marker levels should be the first treatment for all testicular tumors. Organ conserving surgery can be done in synchronous, metachronous or bilateral tumors. This should be followed by chemotherapy.[29]

Testicular germ cell tumors had a cure rate of about 70% with stage I disease and surgery alone. In patients where serological markers are found elevated a wait and watch policy can be adhered to. In cases where the tumor recurs chemotherapy may not be able to give a survival advantage and cure rates as for stage I tumors. Schlatter et al concluded that children with stage I testicular germ cell tumors had an excellent outcome when treated with surgery alone. This was comparable to other studies which have been conducted.[30]

Children with malignant gonadal GCT have been found to have a higher overall and event free survival as compared to other sites. 85% of children studied by Wang et al had germ cell tumor of the testis. Only 33.3% were yolk sac tumors. Of the 59 patients available for follow up, only one had recurrence of disease which progressed to metastasis. This suggests that prepubertal testicular tumors are mostly benign and have an excellent prognosis.[31]

Ovarian GCTs

Ovarian germ cell tumors are more common than testicular germ cell tumors. These present mainly in adolescent girls. The usual presentation is of abdominal distention, pain or a mass. They may present occasionally with acute abdomen which may be a sign of ovarian torsion. Some children will have a workup with ultrasound and tumor markers like AFP and HCG, whereas others who present with an acute abdomen may have a laparotomy which then diagnoses a germ cell tumor on subsequent biopsy[4].

Germ cell tumors have been found in 58% of primary ovarian tumors, in a study conducted in 353 children. These tumors are more likely to be malignant (malignant teratoma, embryonal carcinoma, or dysgerminoma) than those in older patients.[32]

Several studies have shown that a large proportion of these tumors are stage III or IV. The treatment given is a combination of chemotherapy and surgery. Outcome and results have been excellent with 93%- 97% overall survival for all stages as compared to previous studies.[32]

In a study at the University of Texas MD Anderson Cancer centre, malignant ovarian GCTs were treated with upfront surgery followed by chemotherapy with BEP protocol. It was found that a majority of these were dysgerminomas. 95% of these patients were in remission. [33]

Tangir et al studied the reproductive function after fertility preserving surgery and chemotherapy in malignant ovarian germ cell tumors. Fertility preserving surgery involved excising the affected ovary and preserving the contralateral ovary and uterus and tube. Of the 86 women followed up, 38 had attempted conception. It was found that 76% of these women followed up had 1 conception after completing treatment.[34]

Abdominal and Retroperitoneal GCTs

Germ cell tumors of the retroperitoneum can grow to a very large size before they are detected. They are detected by a parent accidentally while bathing a child, or when the child has some trauma. A good number of these are benign teratomas. This poses a problem as these tumors can be abutting major vessels, encasing them or splaying them. Chemotherapy cannot be used to shrink these tumors as these will not respond. AFP and βHCG should be obtained. Confirmation of the diagnosis is by radiological evaluation, and biopsies to rule out malignancy. In tumors which have malignant components chemotherapy can be used to reduce the tumor size so that these can be resected.[1]

Multiple studies have shown abdominal and retroperitoneal tumors to be rare. Malignancy in these tumors is even rarer. The outcome for children with malignant abdominal and retroperitoneal tumors was measured in a study of 57 children by Brodeur et al. They found that stage was the most important factor in determining survival. These children with advanced stages had metastasis to the lungs bone and brain. Radiation was seen to improve survival in children who had non-disseminated GCTs.[35]

Malignancy is observed in 15% of these cases. The mortality for retroperitoneal GCTs was 80% before the advent of platinum based chemotherapy. Billmire et al studied 317 children over a 6

year period of which 26 had malignant retroperitoneal tumors. Most of these children were girls, and despite malignant pathology the outcome was excellent following surgery and chemotherapy.[36]

Germ Cell tumors of the Mediastinum

Germ cell tumors of the mediastinum are rarely encountered. These tumors form a part of the spectrum of nongonadal germ cell tumors. The estimated occurrence is said to be 25% among nongonadal germ cell tumors in children according to some studies. Among these benign tumors teratomas have been found to be the commonest. The malignant germ cell tumors resemble testicular tumors in adults. However the occurrence of malignancy in germ cell tumors of the mediastinum is found to be rare in children.

The following is a clinical staging used in Mediastinal Germ cell tumors. Stage I is well circumscribed tumors with or without focal adhesions to the pleura or pericardium, Stage II is tumor confined to mediastinum with macroscopic or microscopic evidence of infiltration into adjacent structures, Stage III is tumor with metastasis into adjacent intrathoracic organs (Stage III A) and metastasis into extrathoracic organs (Stage IIIB).[4]

In a large study of primary mediastinal germ ell tumors Moran and Suster found that teratomas were most common. However they found that most of these were immature. They also found that among the malignant germ cell tumors, yolk sac tumors were the commonest.[37]

In children mediastinal germ cell tumors can be diagnosed by radiology and tumor markers like AFP and βHCG. Teratoma is the most likely diagnosis in neonates with large mediastinal tumors. However malignancy does occur rarely in adolescents. Surgical resection is the mainstay

in the management of teratomas. Surgery along with chemotherapy is the treatment of choice in malignant GCT's of the mediastinum.[38]

Tumors at miscellaneous sites

Germ cell tumors have been diagnosed in the genitalia, the neck, and the stomach. Genital tumors arise primarily from the vagina. A majority of these tumors were malignant and had a very dismal prognosis. These present with bleeding per vagina, pelvic mass or urinary obstruction. This could be sometimes confused with botryoides type of embryonal rhabdomyosarcoma. Surgical extirpation was the only treatment available despite which the survival rates were low. The introduction of Platinum based chemotherapy has allowed vaginal preservation and survival of more than 80% for these girls.[2,4]

The cervical and facial teratomas present in the neonatal period and most are either mature or immature teratomas. The usual presentation is airway obstruction. Giant tumors may cause hydrops which can cause fetal death. The Ex-utero Intrapartum Treatment (EXIT) procedure can be performed for those without hydrops.[1,4]

Survival and Prognosis of Malignant GCTs

Most studies have shown an excellent survival in resectable teratomas. However teratomas of the mediastinum and retroperitoneum which are unresectable may cause respiratory or cardiac compromise and may lead to the demise in such children.

The introduction of platinum based chemotherapy for the treatment of malignant GCT's has significantly improved survival in children. Low stage tumors of the gonads have almost 100%

survival. Stage III and IV gonadal tumors have a 95% survival. Low stage extragonadal tumors have survival of 90%, whereas Stage III and IV tumors have survival rates of 75%.[2]

Gastric teratomas in neonates have the best prognosis. Antenatally detected teratomas have been found to have mortality rates 3 times higher as compared to those diagnosed postnatally. Among the malignant GCT's patients with Yolk sac tumors and gonadoblastoma were found to have a much better outcome than neonates with choriocarcinoma. Choriocarcinoma has a survival rate as low as 12%. Platinum based chemotherapy has improved survival in neonates and infants with malignant GCT's.[39]

Children with testicular tumors were found to have event free survival (EFS) rates of 85% for stage I; for those who developed a recurrence there was a survival of 100% with salvage chemotherapy. For stage II disease it was found to be 100% 6 year EFS. The 6 year EFS for boys with stage III disease was 100% and 94% for stage IV disease. [8]

Malignant ovarian GCT's have an excellent outcome in children. Billmire et al found six year survival rates of 95% for stage I, 93% for stage II, 98% for stage III and 93% for stage IV tumors where the treatment protocol was followed completely.[18]

The following table shows the event free survival(EFS) and survival in ovarian GCT.[18]

Stage	No	6 Yr EFS%	6 yr survival%
I	41	95	95.1
II	16	87.5	93.8
III	58	96.6	97.3
IV	16	86.7	93.3

The COG/CCG intergroup study found the 4 year event free survival for malignant sacrococcygeal tumors was 84± 6%. They found 4 year overall survival rate of 90± 4%.

The prognosis of malignant testicular GCT's is the best. The overall survival for malignant sacrococcygeal tumors has been found to be around 60% in some studies.[4,39]

The overall outcome was found to be excellent in children with abdominal or retroperitoneal tumors. The POG/CCG study found a 6 year EFS of 82.8± 10.9%, and an overall survival of 87.6±9.3%. Before the advent of platinum based chemotherapy this group had a mortality of more than 80%.[4]

The survival in children with mediastinal tumors was found to be 71±10%. Mortality was seen in children who were over 15 years of age. Yolk sac tumor was found to have a good response to treatment.

The survival of children with tumors at various sites like the genitalia and the cervicofacial region depends on presentation. The tumors of the genitalia have a survival of around 90% according to the COG/CCG study. The tumors of the cervicofacial region are associated with fetal hydrops or with airway obstruction. Although benign the mortality in these tumors is high when associated with hydrops or airway obstruction. [1,2,4]

Special Terminology

Fetus in fetu has been thought to be a highly organized teratoma. Some people argue that it is distinct from a teratoma because of the degree of differentiation and the presence of the axial skeleton. Willis concluded that this was due to the incorporation of a diamniotic monozygotic twin into the body of its partner. Others argue that although placental findings are in favour of twin origin, teratomatous recurrence shows a link in development of fetus in fetu and teratoma.

Cases have been reported of coexisting fetus in fetu and malignant teratoma. According to the WHO classification fetus in fetu is regarded as a mature teratoma. [6,40]

Struma ovarii is the presence of thyroid tissue in a mature teratoma. Malignant transformation can occur rarely, with metastatic disease reported in approximately 20 cases. These tumors can be treated like their thyroid counterparts with cytoreductive surgery and radioiodine ablation.[41]

Growing Teratoma Syndrome is defined as an increase in tumour size during or after chemotherapy for germ cell tumour (GCT), and only mature teratoma at histological analysis of the resected tumour specimen.[2,42]

Malignant transformation has been reported frequently in benign and immature teratoma. These tumors which recur and have malignant transformation are very aggressive. The frequency of malignant transformation mandates long term follow up in all teratomas especially the ones which have immature elements. Large tumors with immature elements have a high chance of malignant transformation. Malignant transformation has been seen in cervical teratomas, mediastinal, retroperitoneal, gonadal and sacrococcygeal teratomas.[43]

Recent Advances

Various advances have been made in the treatment of germ cell tumors whether it concerns diagnosis, treatment which may be single modality or multidisciplinary. All these have improved the survival in children with germ cell tumor.

Germ cell tumors can be diagnosed antenatally. This has been made possible by the advent of high resolution ultrasound. In-utero diagnosis is made possible for sacrococcygeal teratomas. Most of these tumors are benign but some may have a yolk sac tumor component.

The mortality from fetal sacrococcygeal teratomas is very high. This occurs in fetuses which develop hydrops or if the tumor is diagnosed before 30 weeks of gestation. The ex-utero intra-partum treatment (EXIT) procedure is used to debulk this tumor to prevent the arterio-venous shunt which occurs due to the bulk of these tumors.[6]

The introduction of various imaging techniques for diagnosis of germ cell tumors can describe the area of the tumor, any local extension and distant metastasis. Computed Tomography scan(CT) and Magnetic Resonance Imaging (MRI) are now regularly used to determine the extent of tumor. Three Dimensional imaging has now come into vogue with the advances in MRI and CT imaging. 3-D imaging is used to map the tumor its extent blood supply and treatment.[13,44,45]

The tumor markers AFP and βHCG are now used not only to diagnose malignant germ cell tumors but also the response to therapy. Persistently elevated level of markers suggests non response to therapy. Steady decline with normal levels of markers suggests complete response. Elevation after an initial fall suggests resurgence or incomplete response to therapy.[1,2,4]

Introduction of platinum based chemotherapy has improved survival in children with malignant germ cell tumors. The Children's Cancer Group (CCG) and the Pediatric Oncology Group (POG) have established and improved on protocols which have been formulated in the last decade which have helped improve survival to very significant level. The introduction of these protocols has increased survival to above 95% for most stages of malignant GCT's compared to a survival of 50-60% previously. The survival of children with tumors especially of the genitalia was dismal and rates were as low as 30% in some studies.[1,14,26,33,35,45–47]

The introduction of Flouro-Deoxyglucose Positron Emission Tomography has added a new dimension to the management of malignant germ cell tumors. The use of PET has not been fully

realized in the treatment of germ cell tumors. PET scans have been found to be superior to CT for residual tumors and also for response to therapy. The limiting factors for its use is the availability and cost.[48]

MATERIALS AND METHODS

Study Design

This is a retrospective study of all children below 16 years of age who were diagnosed to have extracranial germ cell tumors (GCTs) in the department of Paediatric Surgery, Christian Medical College and Hospital between January 2003 and December 2012.

Patients

107 children, below the age of 16 years, who were diagnosed to have extracranial germ cell tumors, between January 2003 to December 2012, were included in this study.

Data Collection

All the patients or their relatives were informed by phone or by mail by the investigator, and enquiries made into their present status and outcome. For all patients who followed up a consent was obtained. A proforma was filled by the investigator. The operative records, investigations and follow up records were collected from the hospital database and records and reviewed and also included in the proforma. This data was tabulated into Microsoft excel worksheet and then analyzed as such using demographic, clinical, biochemical and radiological parameters.

Data Analysis

Descriptive statistics were reported using Mean±SD/ Median (IQR) for continuous variables. Categorical variables were reported using Frequency and Percentage. Chisquare /Fisher's exact test and two independent Sample t test/ Mann Whitney's U test were used to assess the variables. Binary Logistic Regression was used to look at the risk factors associated with mortality. Overall Survival (OAS) and Event Free Survival (EFS) were estimated using Kaplan Meier survival curves. Log rank statistics was used to assess the significance of the factors associated with OAS and EFS. P value <0.05 was considered to be statistically significant. Analysis was done using SPSS 16.0.

Exclusion Criterion

Children who had intracranial germ cell tumors

RESULTS

Christian Medical College had a total of 1532840 patients in OPD in 2011 of which approximately 66040 were seen in Child health OPD. Paediatric surgery had 17000 patients and paediatric oncology had 8500 patients. Approximately 100-120 patients were admitted for treatment of paediatric solid tumors every year, of which 8-10 had germ cell tumors (GCT).

All children below the age of 16 years, diagnosed to have extracranial Germ Cell Tumors (GCTs) from January 2003 to December 2012 were recruited into this study.

A total of 107 children were diagnosed to have extra cranial GCT from January 2003 to December 2012 who presented to the department of Paediatric surgery.

The age ranged from a day old neonate to 14 years. 29 children were less than one year of age, 31 were between 1 and 5 years. 22 children between 5 and 10 years and 25 were more than 10 years of age at the time of diagnosis. 38 of these children were male and 69 were female.

Figure 1: Age Distribution of Germ Cell Tumors (GCTs)

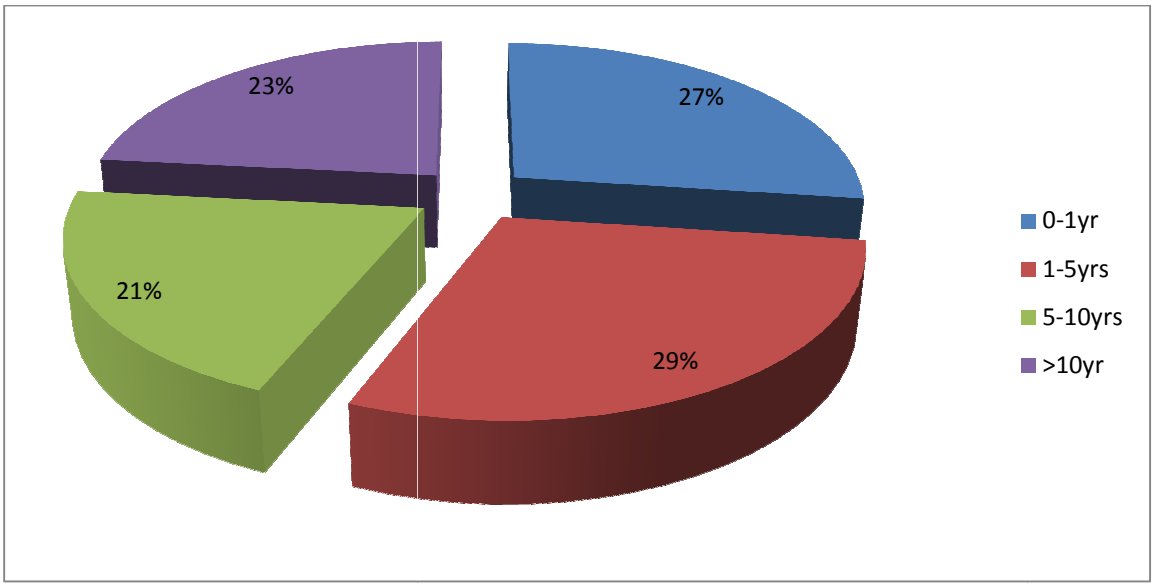


Table 1: Distribution of GCTs According to Site and Age.

Site / Age	0-1year	1-5 years	5-10years	>10years	Total
Testicular	4	7	1	5	17
Ovarian	0	4	13	13	30
Sacrococcygeal	13	7	5	0	25
Retroperitoneal	5	9	1	1	16
Abdominal	3	2	0	2	7
Thoracoabdominal	1	0	0	0	1
Mediastinal	0	1	1	3	5
Miscellaneous	3	1	1	1	6
Total	29	31	22	25	107

47 (44%) children had gonadal GCT comprising the largest group in this study. 25 (23%) children had sacrococcygeal tumors, 16 (15%) had retroperitoneal, 7 (6%) had intra-abdominal tumors, 5 (5%) had mediastinal, 1 (1%) had thoracoabdominal and 6 (6%) had tumors at miscellaneous sites like the neck, vagina, bladder etc.

Figure 2: Distribution of GCTs according to site

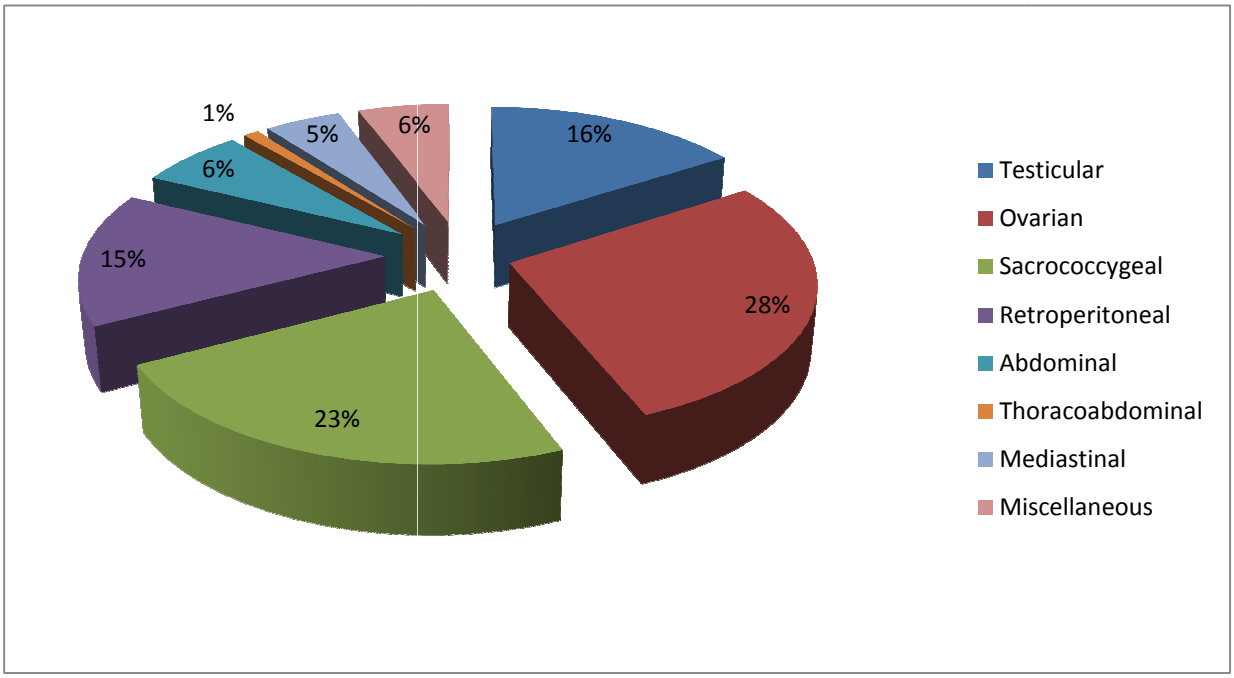
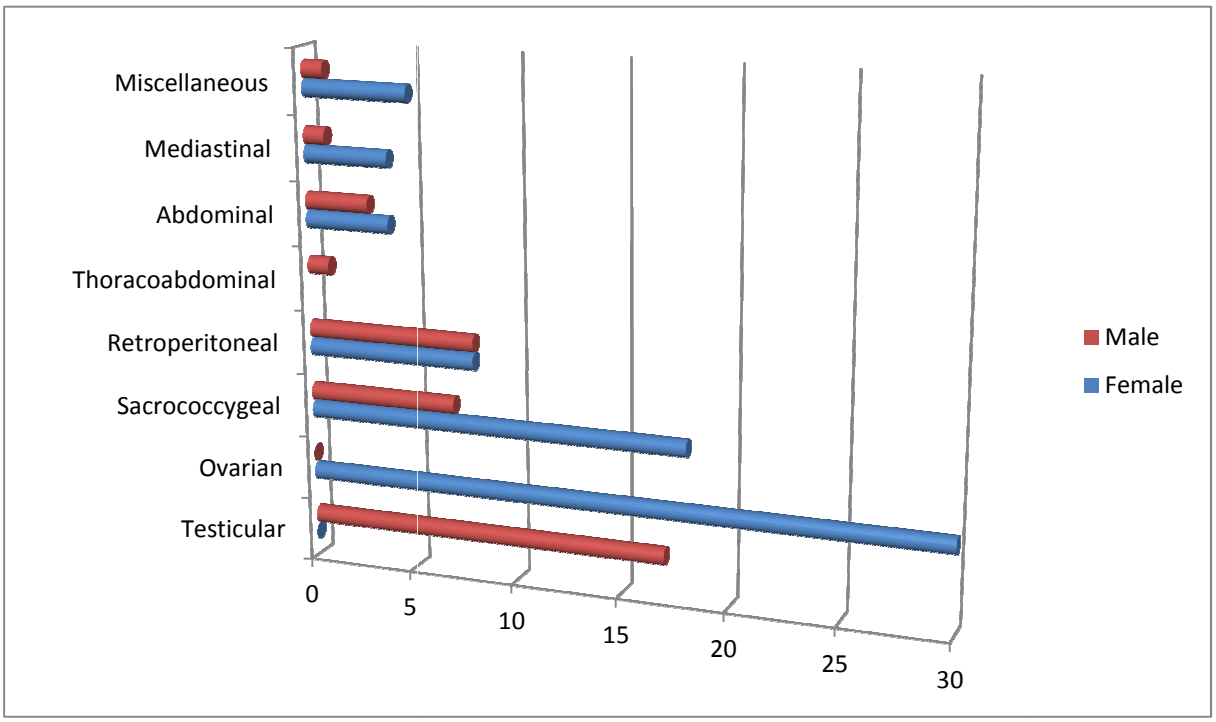


Figure 3: Distribution of GCTs According to Gender



49 of the 107 children had malignant tumors, 49 had benign tumors and 9 had immature teratomas. 13 of the 17 children with testicular tumors had malignancy, 19 of the 30 children with ovarian tumors had malignancy, and 8 of the 25 children with sacrococcygeal tumors had malignant components. Malignancy was seen in 3 of the 16 children with retroperitoneal tumors, the rate of malignancy among the children with abdominal tumors was 1of 7. 1 child with the thoracoabdominal tumor was diagnosed to have a malignant tumor. All the mediastinal tumors were benign. 4 of the 6 children with tumors at miscellaneous sites had malignancy.

Figure 4: Distribution of GCTs According to Histology

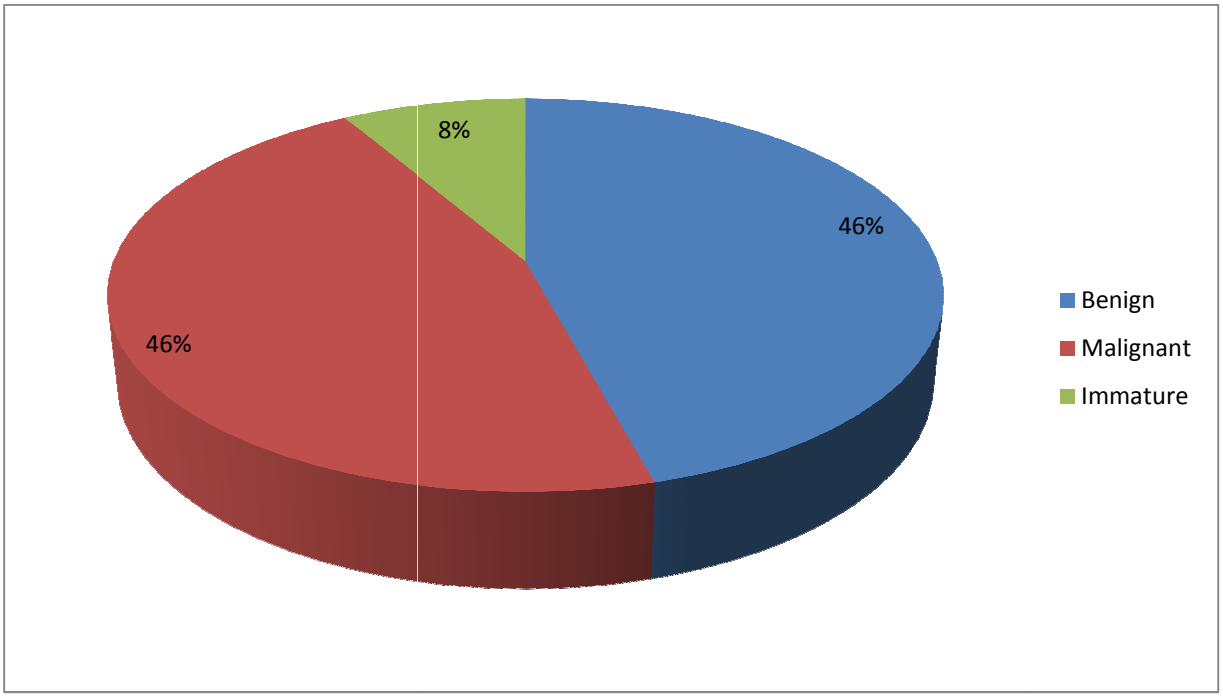


Table 2: Distribution of GCTs according to Histology

	Malignant	Benign	Immature	Total
Testicular	13	3	1	17
Ovarian	19	9	2	30
Sacrococcygeal	8	15	2	25
Retroperitoneal	3	11	2	16
Abdominal	1	4	2	7
Thoracoabdominal	1	0	0	1
Mediastinal	0	5	0	5
Misc	4	2	0	6
Total	49	49	9	107

Histopathology Pictures of GCTs

Figure 5: Mature Teratoma

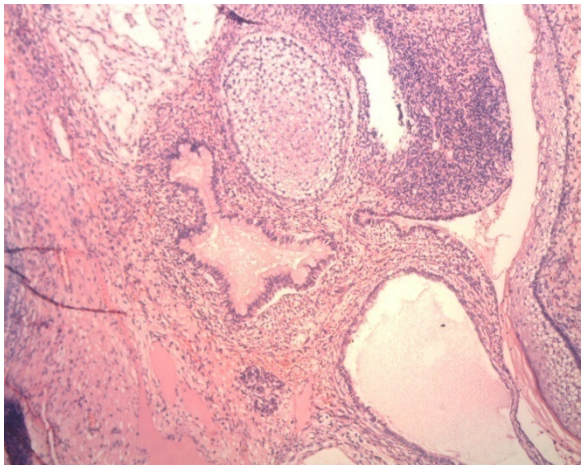


Fig 6: Yolk Sac tumor

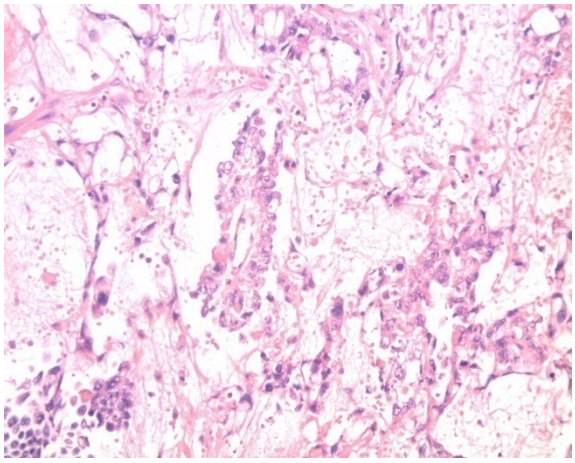


Figure 7: Dysgerminoma

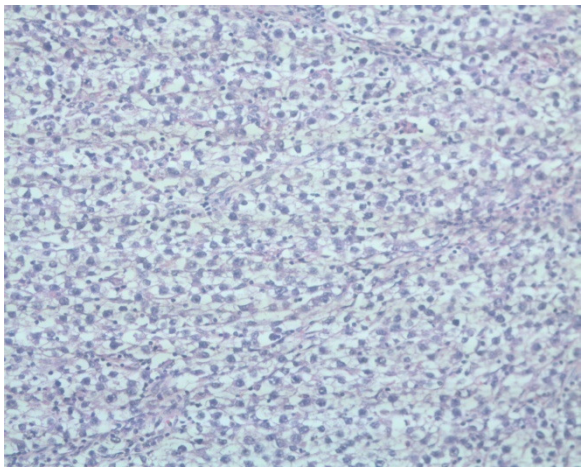


Figure 8: Immature Teratoma

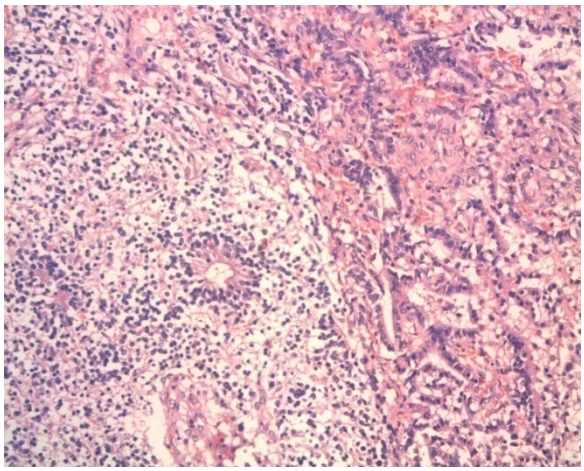


Fig 9: Embryonal Carcinoma

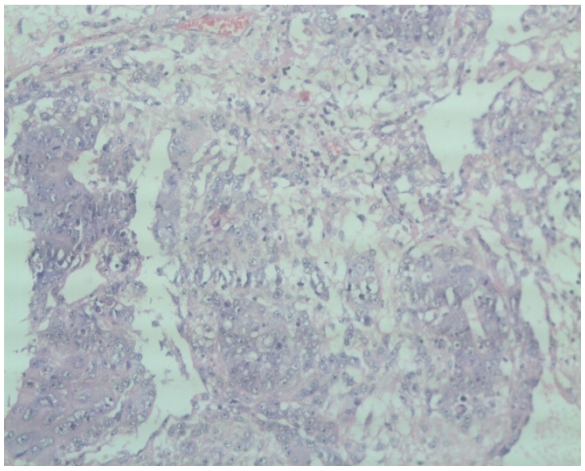
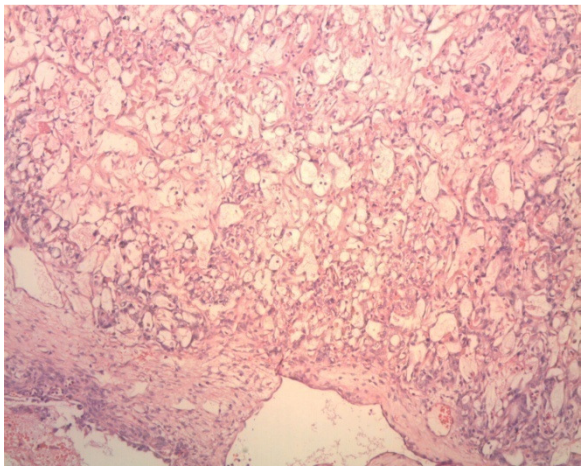


Figure 10: Yolk Sac Tumor Testis



All Children with malignant GCTs had an elevated AFP. In some ovarian GCTs β HCG was also elevated. The elevation ranged from a few hundreds to a few lakh IU/ml (range300-1000000 IU/ml). The AFP levels decreased consistently with treatment in the malignant GCT. This will be discussed in detail in the specific tumor sections.

The overall survival was 95% for all GCT's. The median survival was 50 months. Median survival among females was 51 months and for males was 44 months. The median survival for children with benign GCT was 58 months, for immature GCT was 48 months and for malignant GCT was 44 months (p=0.020). Overall survival for malignant GCT was 85.2%

Figure 11: Cumulative Survival in GCTs

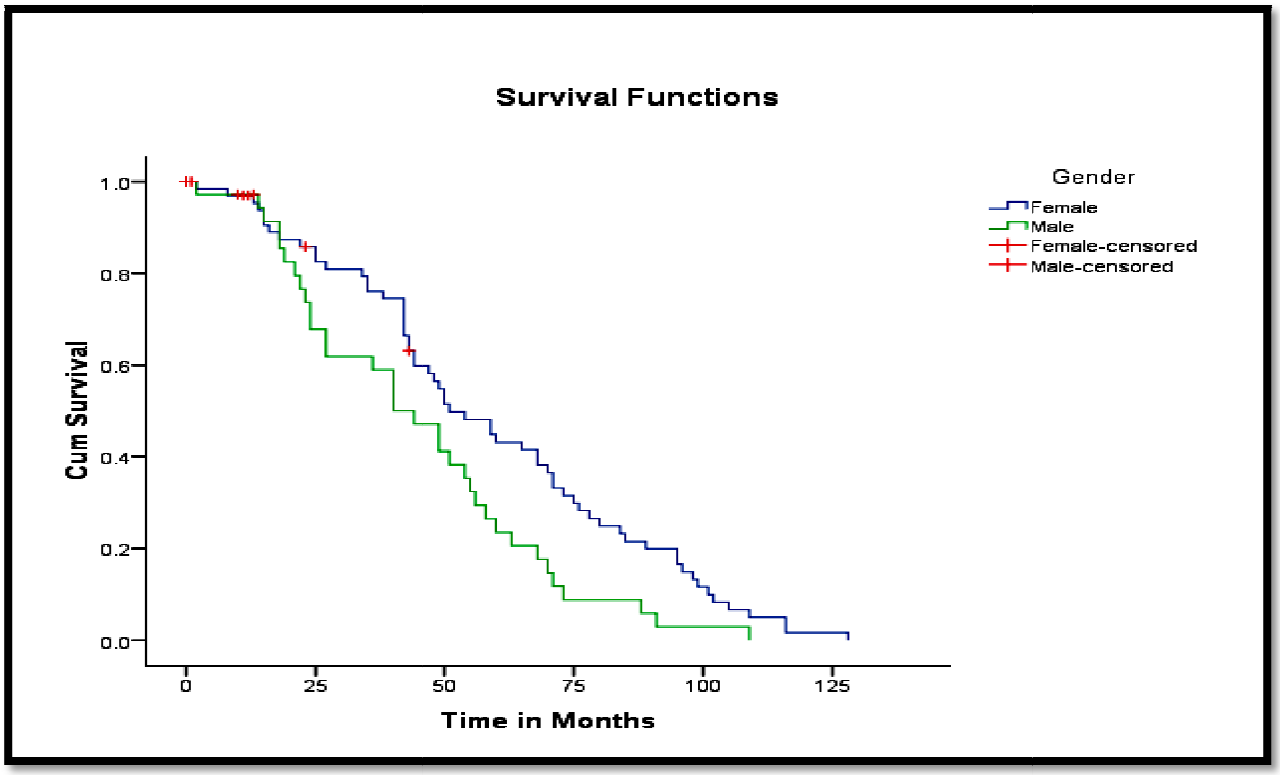
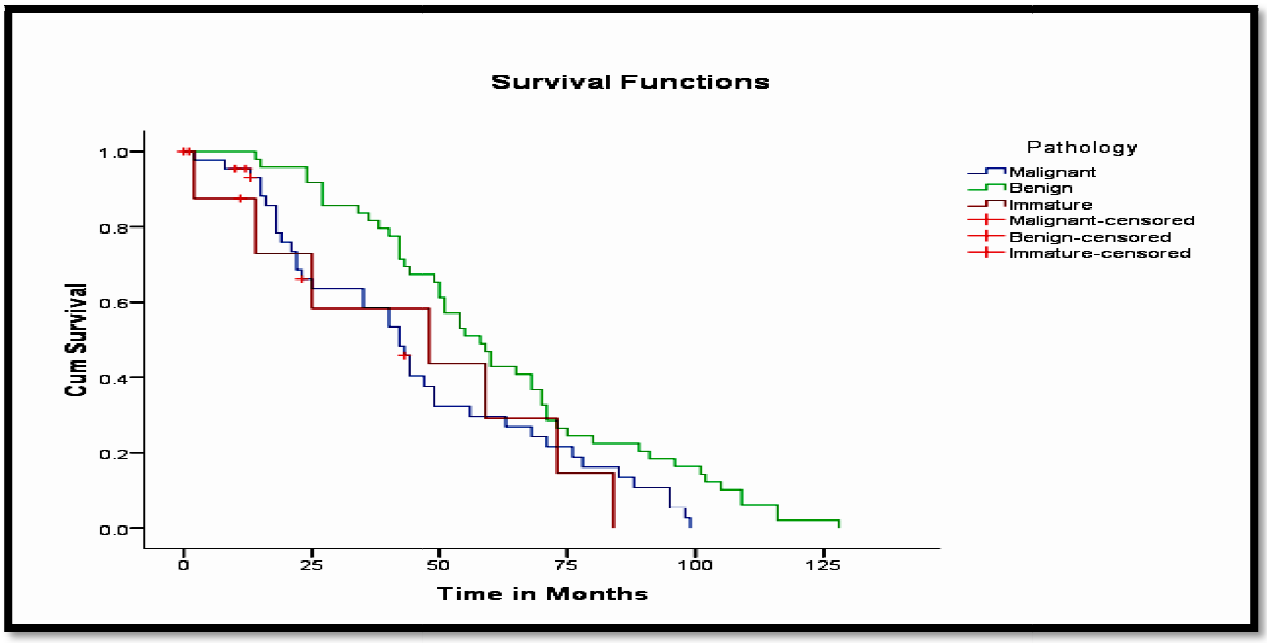
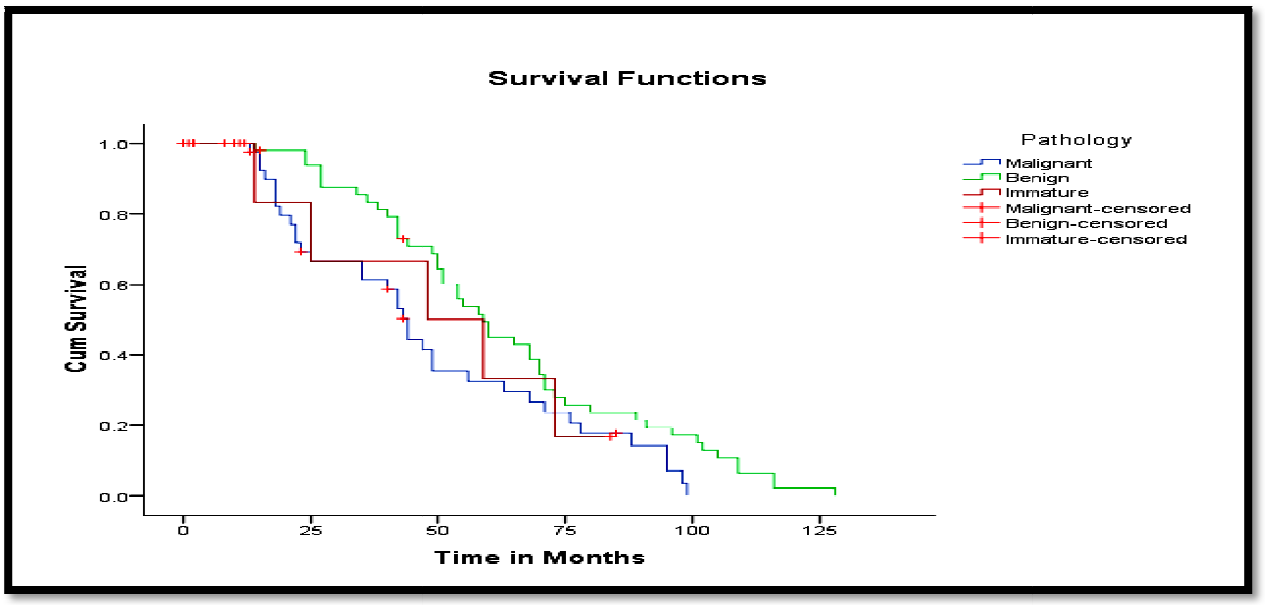


Figure 12: Survival against Histology in GCTs



Event free survival in all GCTs was 85%. The event free survival in females was 85% and in males was 84%. The event free survival in malignant GCT was 75.9%, in immature teratomas was 87.4% and for benign tumors was 100%.

Figure 13: Event Free Survival in GCTs



Testicular Germ Cell Tumors

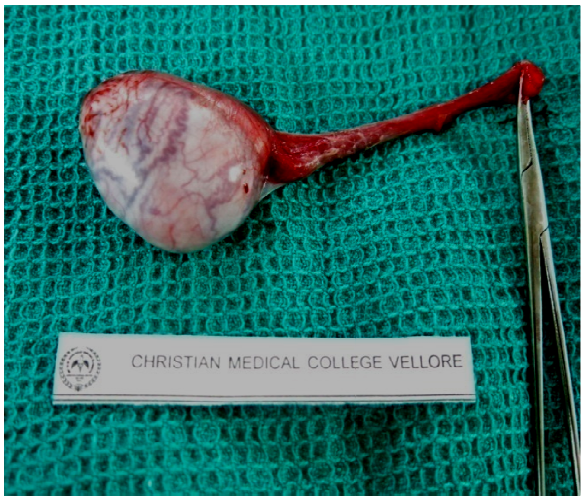
Boys with testicular tumors formed 17% of the patients studied with GCT.

Table 3: Age distribution of children with Testicular Tumors

Age	0-1 years	1-5years	5-10years	>10years	Total
Number(n)	4	7	1	5	17

16 (94%) of the 17 boys who presented with a testicular tumors had a mass of the side of the scrotum which was enlarging. 1 child who had an undescended testis, presented with abdominal pain and vomiting and was found to have an intra-abdominal testis which had undergone torsion. This tumor was malignant. 1 child presented with abdominal distention in association with an enlarging scrotal mass.

Figure 14: Testicular Germ Cell Tumor in a 2 year old boy



Of the 17 boys, 13 (76.5%) had malignant GCT 3 had benign teratomas and 1 had an immature teratoma.

Figure 15: Distribution of Testicular GCT according to histology

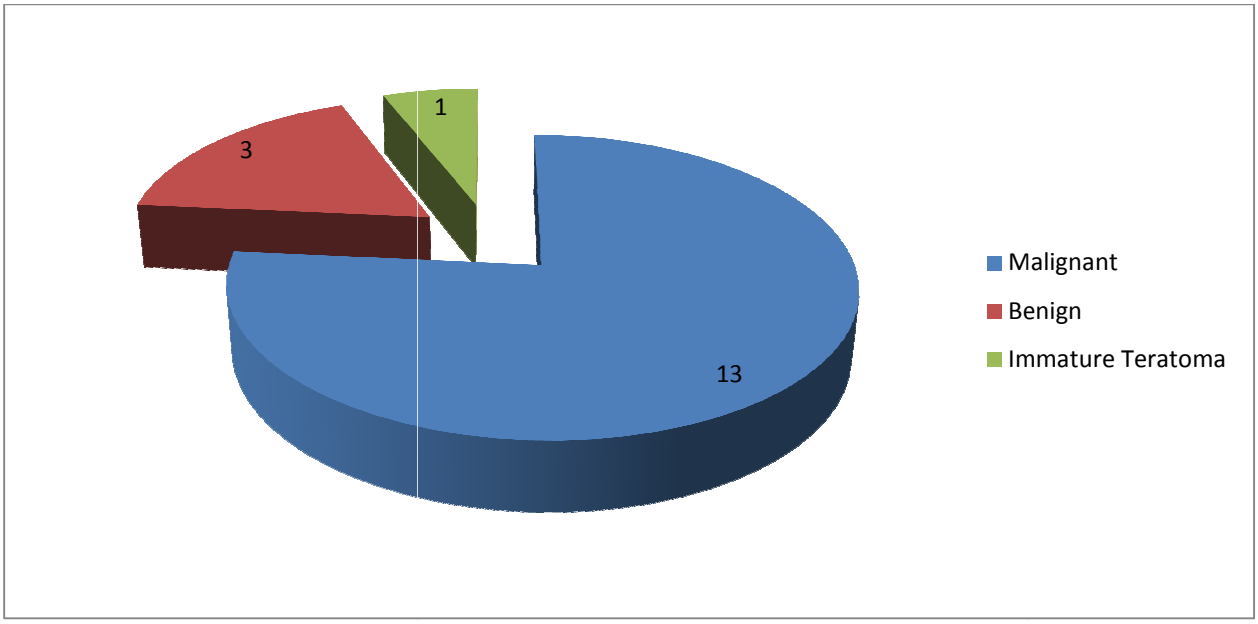


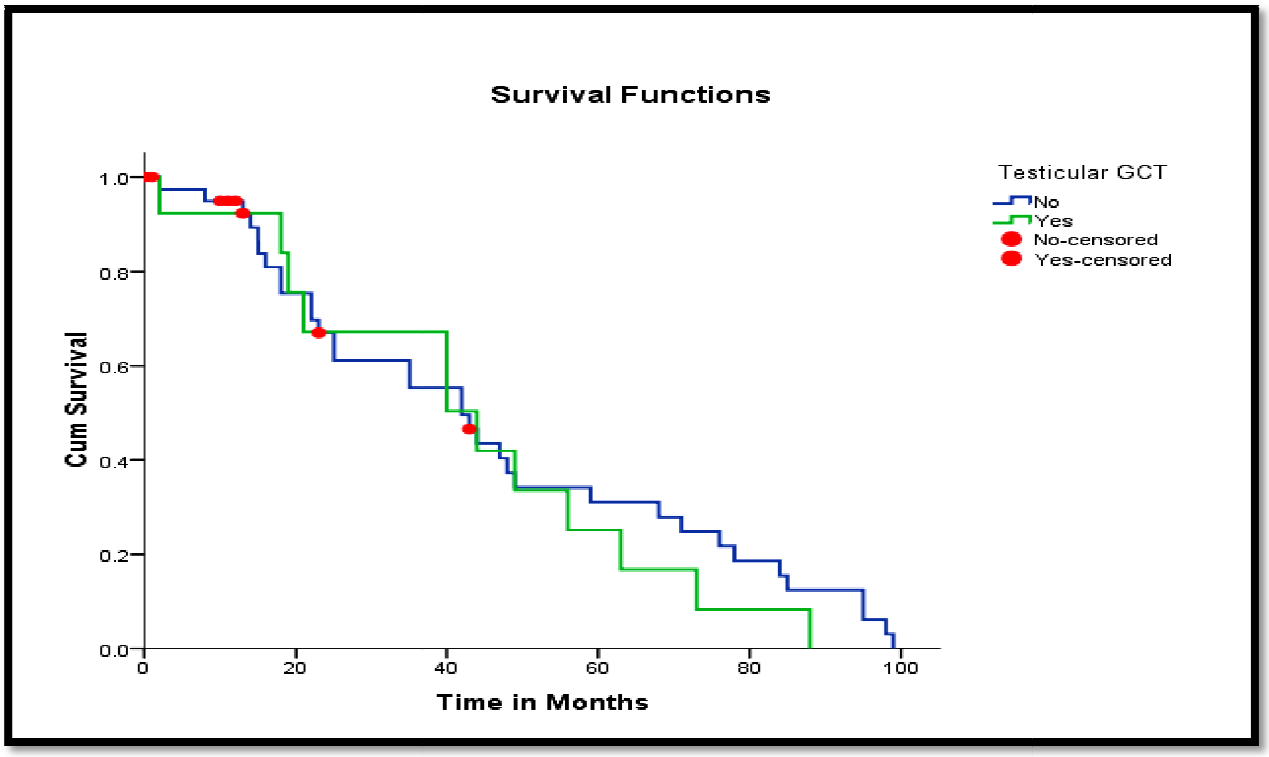
Table 4: Distribution according to Histology in Testicular GCT

Histology	Benign	Yolk Sac Tumor	Embryonal Carcinoma	Mixed Malignant Germ Cell Tumor	Non Seminomatous GCT	Immature Teratoma
Number	3 (17.6%)	10 (58.8%)	1 (5.8%)	1 (5.8%)	1 (5.8%)	1 (5.8%)

Treatment given was a high orchiectomy followed by 6 cycles of JEB (Carboplatin, Etoposide and Bleomycin) in 12 (85%) children. This was followed by IVAD in 1 and IVeP in one child. 1 child had abandonment of treatment as there was extensive metastatic disease.

Overall survival was 85.7% for children with malignant testicular GCT. Event free survival was 71.4%. 1 child had abandonment of treatment as there was widespread metastatic disease. Follow up ranged from 12-108 months. Median survival was 49 months. All the children who survived showed adequate growth for age and had no follow up problems which included renal and respiratory function.

Figure 16: Overall Survival in Malignant Testicular GCT



Ovarian Germ Cell Tumors

30 girls presented with ovarian germ cell tumors. These constituted 26.4% of all children with germ cell tumors. The most common presenting feature was pain which was seen in 66.6% (n=20) patients. This was followed by a mass in association or in isolation in 50% (n=15) patients. 13% (n=4) had associated vomiting. 1 child presented with associated fever and loss of weight, 1 with abdominal distention and 1 with ascites.

Screening radiology showed the size of the mass the extent, but it was difficult to tell the originating side of the ovarian mass due to the size of some of these tumors. The masses ranged from 4cm by 3 cm to 19cm by 10 cm and in some cases occupied most of the peritoneal cavity.

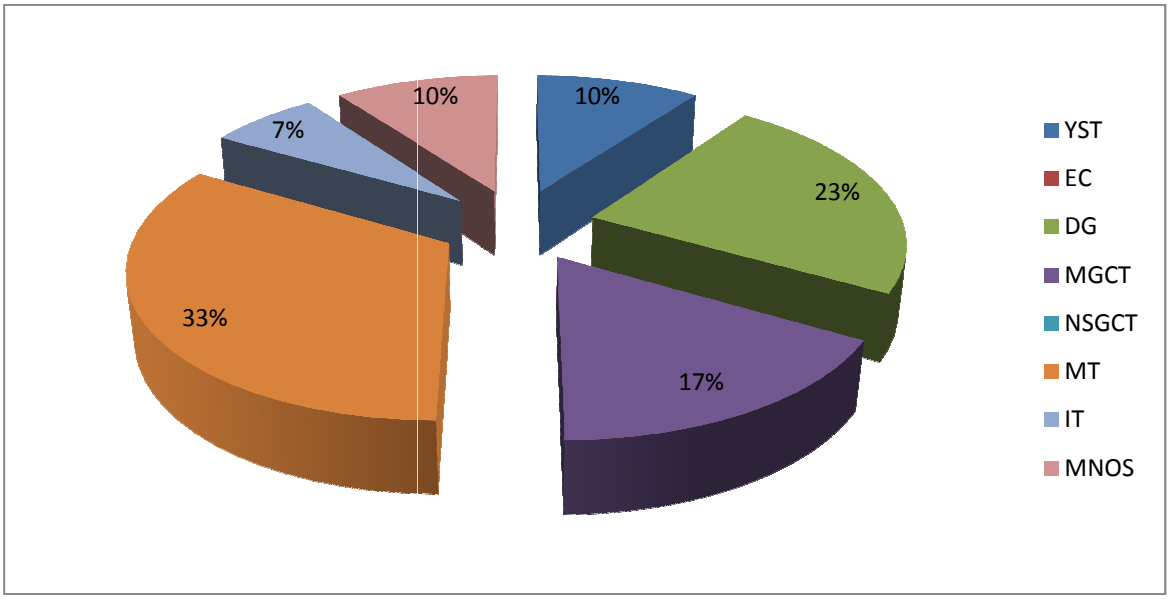
Follow up screening radiology showed residual masses post chemotherapy in these children. The size of these masses had become half to one third of the original in a majority of these children.

Operative findings were consistent with the radiological findings. A unique feature in 3 children was that they had torsion with gangrene of the ovary.

18 (60%) of these girls had malignant germ cell tumors and 12 (40%) had benign teratomas of the ovary. The AFP was elevated in all the children with malignant GCT. AFP ranged between 88- >1000000 IU/ml. βHCG was raised in 10 patients. Range was from 27.8-196900 IU/ml.

The diagnosis was based on tumor markers and radiological findings in most. 15 (83%) of the 18 children were treated based on tumor markers. 3(16%) were treated for malignancy following a laparotomy for acute abdomen in which torsion of ovarian mass was found and subsequent biopsy exhibited a malignant GCT.

Figure 17: Distribution of Ovarian GCT according to Histology



YST- Yolk Sac tumor, EC- Embryonal Carcinoma, DG-Dysgerminoma MGCT- Mixed GCT, NSGCT- Non seminomatous GCT, MT-mature teratoma, IT-immature teratoma, and MNOS-malignant GCT not otherwise specified.

2(13.3%) of the children with malignant disease were treated with PEB chemotherapy (Cisplatinum, Etoposide and Bleomycin) and 16 (86.6%) were treated by the JEB protocol. The children who received preoperative chemotherapy were treated with 4-6 cycles of preoperative followed by 2-4 cycles of the same chemotherapy post operatively. 1 child had a recurrence after primary treatment and was given VeIP (Etoposide, Ifosphamide and Cisplatinum) cycle post primary chemotherapy and surgery.

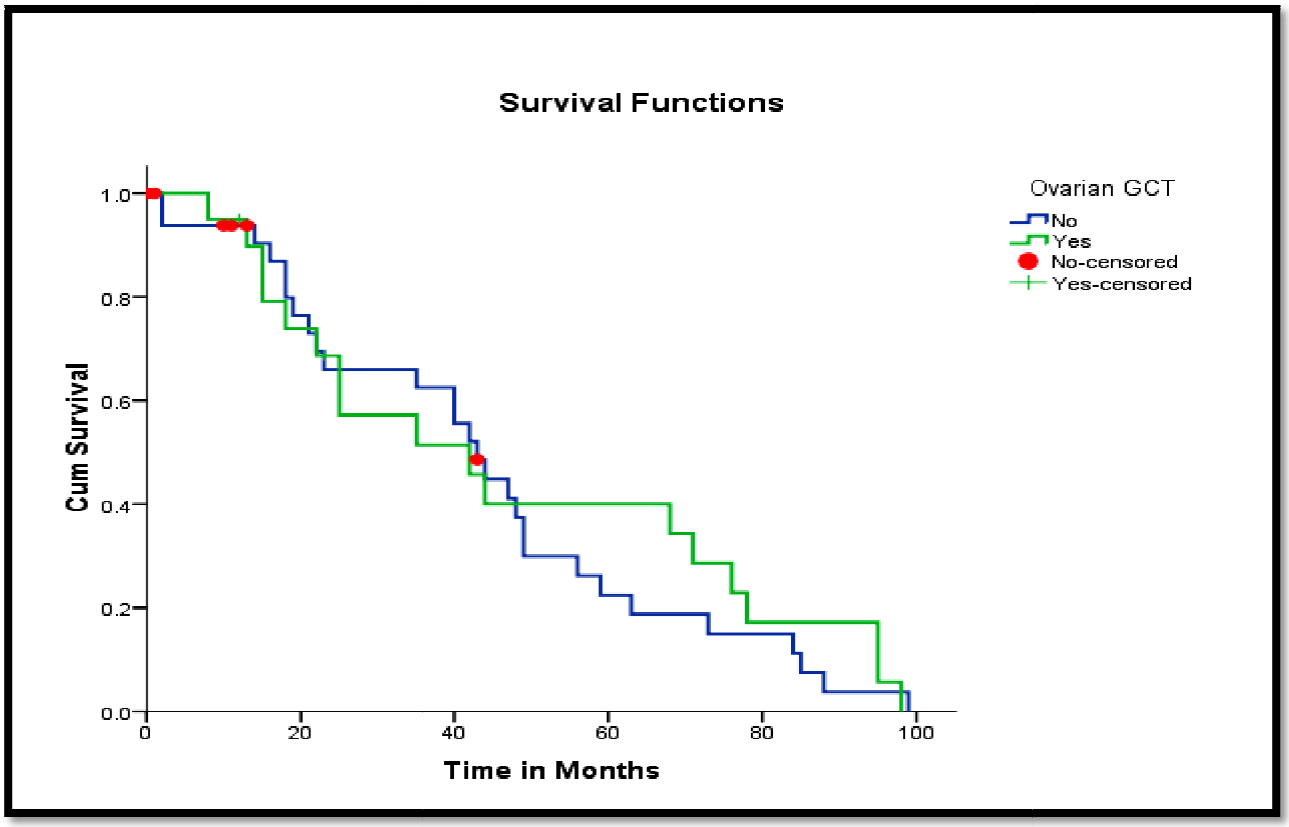
Table 5: Trends of AFP levels once therapy was initiated and at follow up

AFP (IU/ml)	At Diagnosis	Post Chemotherapy	Post Chemo/Surgery	At completion/follow up
0-50	6	8	14	17
50-100	1	0	0	0
100-1000	1	5	2	0
1000-10000	2	1	1	0
10000-100000	6	2	0	0
>100000	2	1	0	0

The children with ovarian GCT had a good overall survival in this study. 28 of the 30 girls survived. 2 children had abandonment of treatment. Both had recurrent metastatic disease which was non-responsive to chemotherapy.

Follow up ranged from 2 months to 120 months with a median survival of 44 months. Overall survival (OS) in those with malignant ovarian GCT was 90% and the event free survival (EFS) was 85%. The children who have survived have shown an adequate growth pattern. A number of them have attained menarche. 1 of the patients is married and has 2 children, 5 years after completion of treatment. 1 child has ovarian failure, has failed to attain menarche, and has not developed secondary sexual characters.

Figure 18: Overall Survival in Malignant Ovarian GCT



Sacrococcygeal Teratoma (SCT)

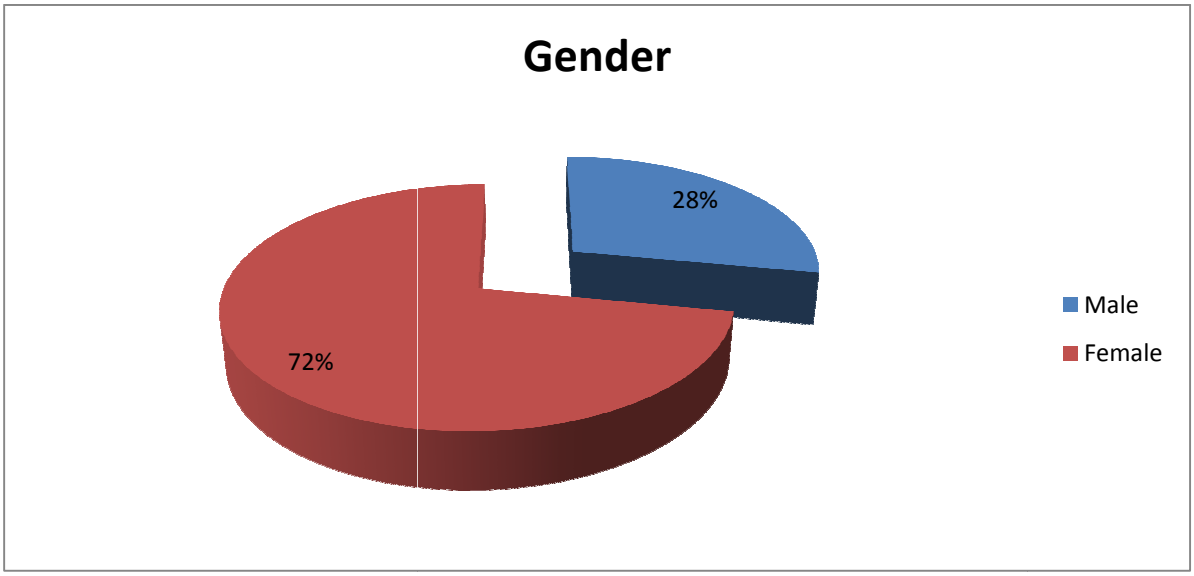
There were 25 children who presented with sacrococcygeal teratoma constituting 23% of children in this study. 7 (28%) of these children were male and 18 (72%) were female. 4 (16%) children presented at birth. 8 (32%) presented by 1 year of age. 12 (48%) presented between 1 year to 10 years of age.

Figure 19: A New Born with Sacrococcygeal Teratoma (SCT)

Table 6: Age distribution in Sacrococcygeal Teratoma (SCT)

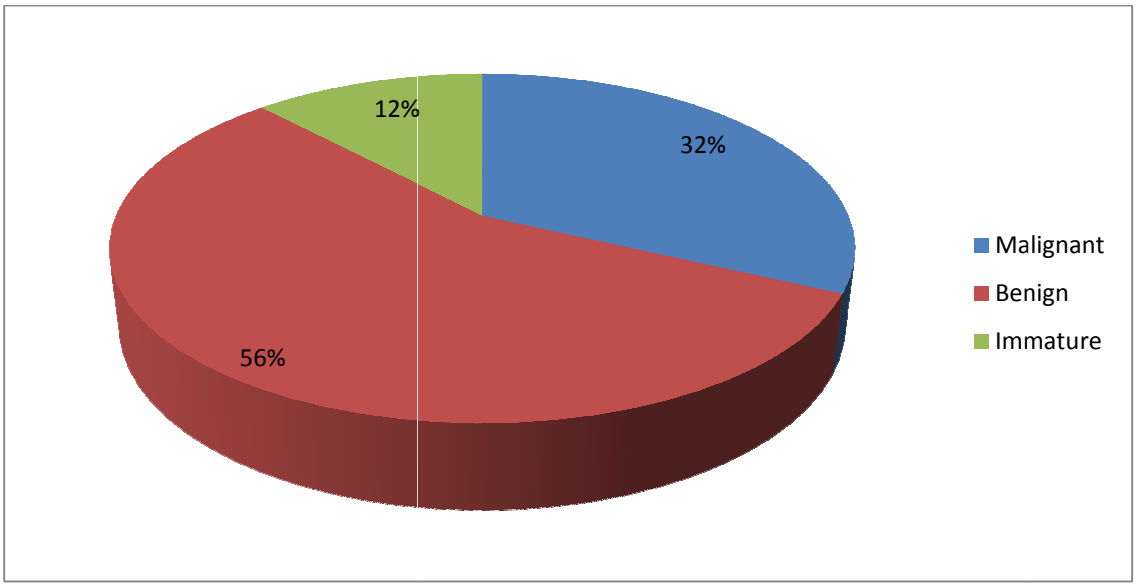
Age (years)	Number(n)	Percentage (%)
0-1	8	32
1-5	12	48
5-10	4	16
>10	1	4
Total	25	100

Figure 20: Gender Distribution of SCT



14 (56%) children had benign tumors, 8 (32%) had malignant components and 3(12%) had immature elements. Of the children with malignancy 5(62.5%) were females and 3(37.5%) were males.

Figure 21: Percentage Distribution according to Histology in SCT



24 (96%) of the children with SCT presented with a sacrococcygeal mass. 1 child had pain with no visible mass. Associated features at presentation were paraparesis in 1 child, and multiple sinuses in 1 child. One child had been operated at birth but the mass had recurred after 7 months, 1 child had a sudden increase in the size of the mass, and 1 had a biopsy of the mass before presentation, 1 child had presented with a neurogenic bladder and 1 with weakness of the rectal sphincter and was incontinent to stools.

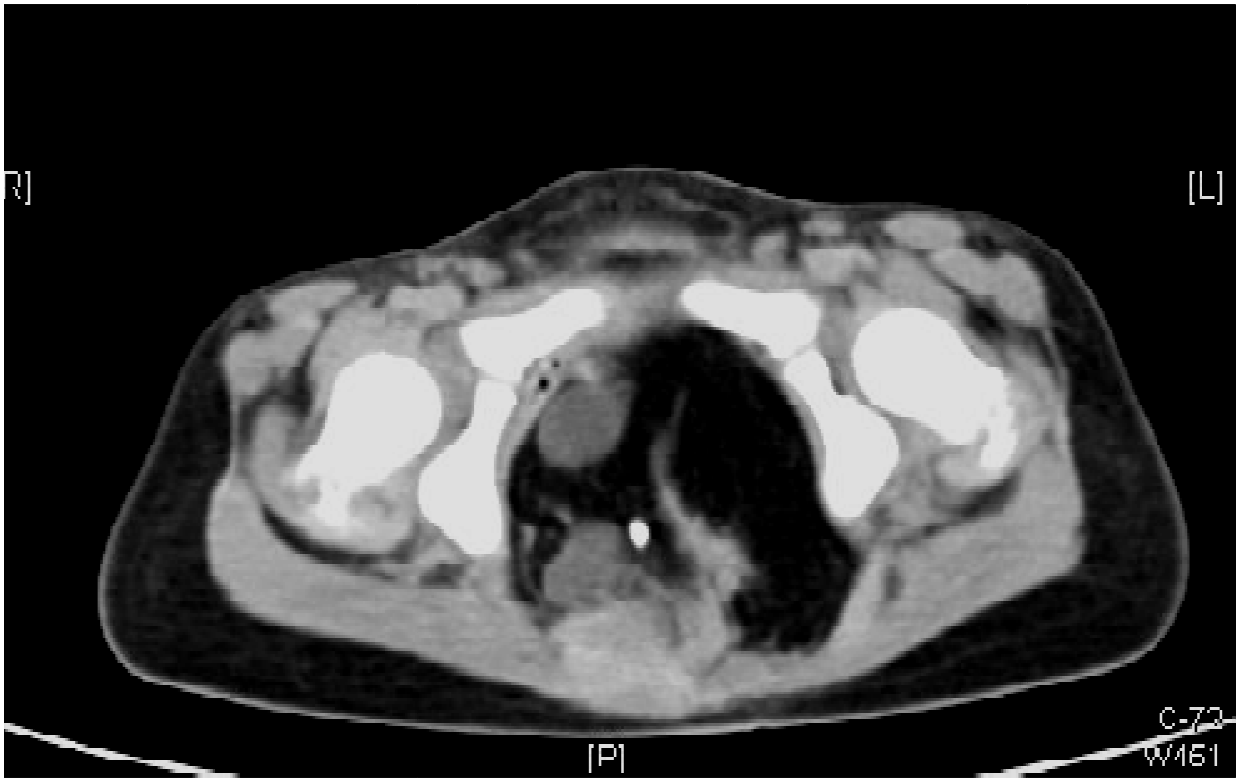
Table 7: Associated Symptoms in SCT

Symptom	Pain	Paraparesis	Sinuses	Neurogenic bowel and bladder	Sudden increase in size of mass
Number	1	1	1	2	1

Table 8: Distribution According to Altman Classification of SCT

Altman Type	Number	Percentage of total	Percentage Malignant
I	10	40%	0%
II	7	28%	14%
III	6	24%	83%
IV	2	8%	100%

Figure 22: CT Scan of an Altman Type III SCT



The tumor size ranged from 1.4 cm by 4 cm to as large as 20 cm by 15 cm in size.

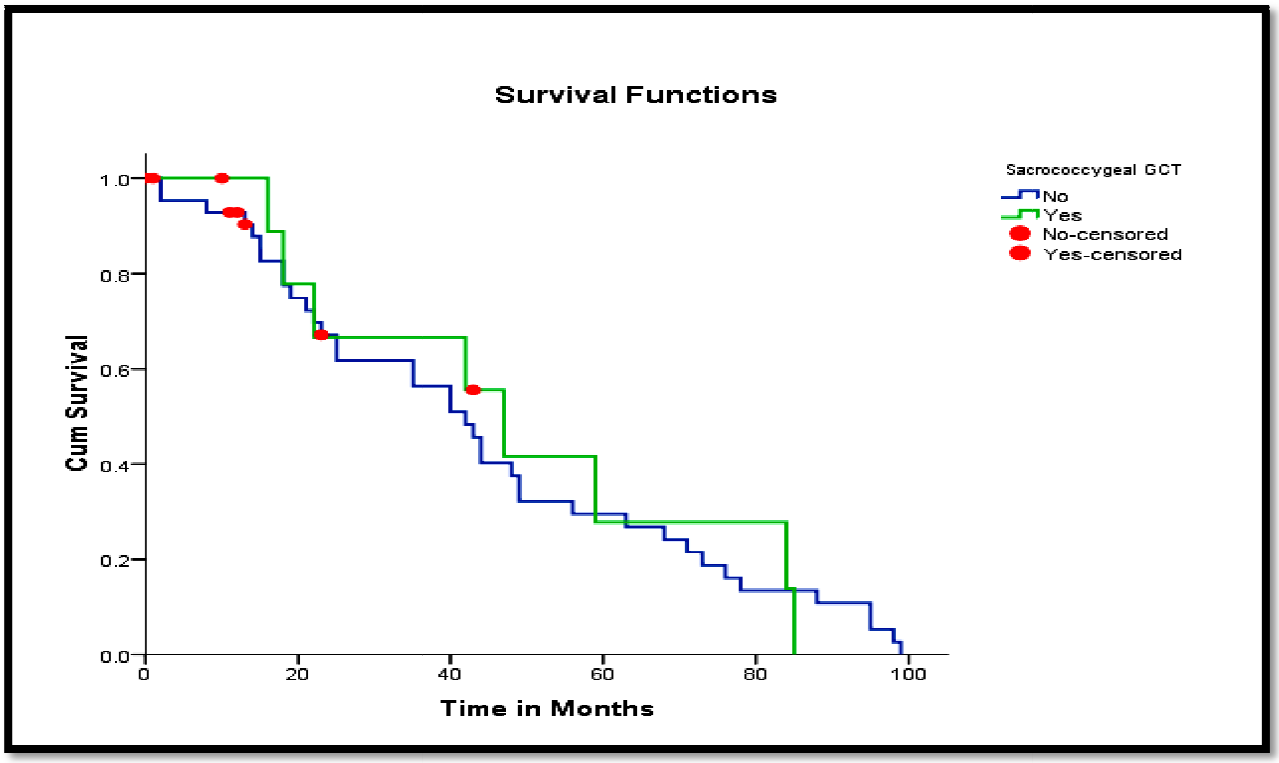
All 8 (100%) children with malignant SCT had elevated AFP. AFP levels ranged between 816 IU/ml to 140800 IU/ml. This value decreased consistently with treatment including surgery and

chemotherapy. 2 (66%) of the 3 patients with immature teratomas had raised AFP. Range was 3.14IU/ml to 30000IU/ml.

Follow up ranged from 12 months to 120 months. 2 of the children with SCT died. 1 child died one year after diagnosis, the other died 4 years after completion of treatment of unrelated causes. The overall survival was 92% and EFS was 80%. OS in malignant SCT was 80% and EFS was 60%.

Some of these children have residual problems. 3 (12%) children have neurogenic bladder, 1 child has weakness of the rectal sphincter, and 1 child has developed a hemoglobinopathy and is on treatment.

Figure 23: Survival in Malignant Sacrococcygeal GCT



Retroperitoneal GCT

16 children of the 107 had retroperitoneal teratomas. This constituted 15% of the total study population. 8 (50%) were girls and 8 (50%) were boys. Age at presentation ranged from 2 months to 14 years. Mean age was 32 months.

Table 9: Age Distribution of Retroperitoneal GCT

Age(years)	0-1	1-5	5-10	>10	Total
Number	5	9	1	1	17

Table10: Distribution of Symptoms in Retroperitoneal GCT

Symptom	Mass	Percentage
Number	12	75%
Abdominal Distension	9	53%
Pain	4	25%
Vomiting	1	6%
Paraparesis	1	6%

Radiological screening by way of CT scan or Ultrasound of the abdomen was done for these children. The tumor size ranged from 6cm to 15 cm diameter. 2 (12.5%) of these tumors were present on the right of the midline, 9 (56.25%) were midline tumors, and 5 (31.25%) were present on the left of the midline. 2 were in relation to the left kidney and 2 in the right suprarenal region. 1 child had metastasis to the liver.

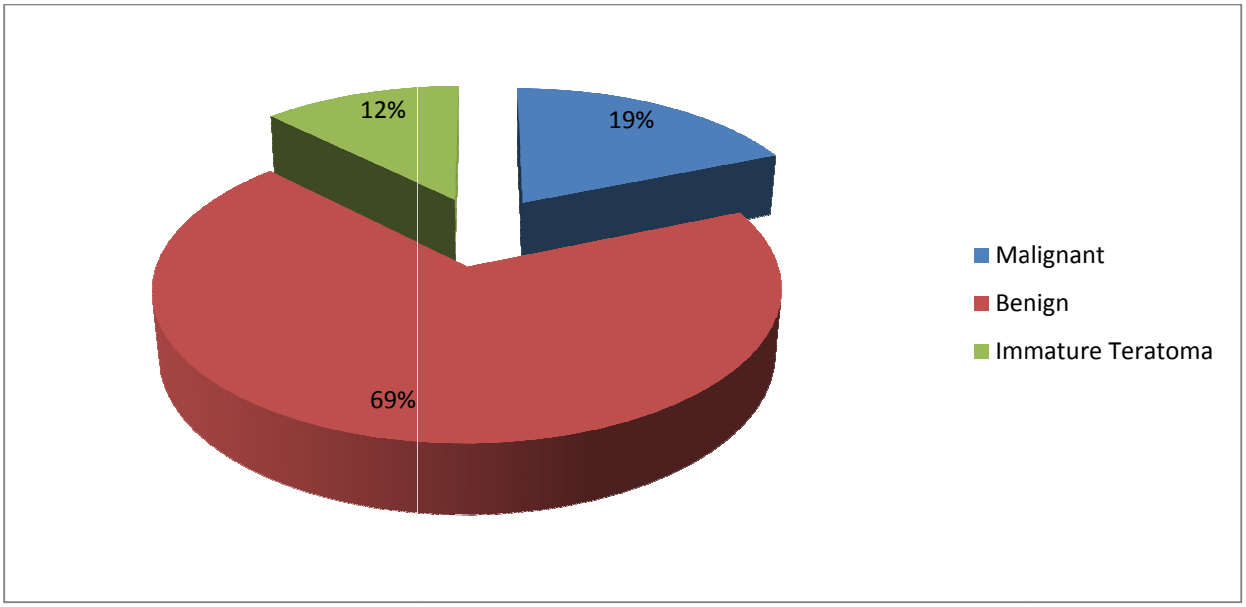
Figure 24: Pretreatment CT scan in a Malignant Retroperitoneal GCT

Figure 25: Post Chemotherapy CT Scan for the same patient

11(68.8%) children were diagnosed to have benign lesions and 3 (18.7%) had malignant lesions. 2(12.5%) child had an immature teratoma. AFP was elevated in the children with malignant neoplasm. It ranged from 139 IU/ml to >30,000 IU/m.

3 of the children with malignant neoplasms were given 4 cycles of JEB chemotherapy, 1 child with immature teratoma was given four cycles of JEB. Values of AFP followed a decreasing pattern with chemotherapy. There was a significant reduction in size of the tumor following chemotherapy in all the children with malignant GCT. The size ranged from 2 cm to 7cm in largest diameter as compared to 6cm to 15 cm pre chemotherapy.

Figure 26: Distribution According to Histology in Retroperitoneal GCT



Surgery was performed as an adjunct in children with malignant disease and primarily in children with benign disease. 17 of the children had complete excision of tumor. Surgery had to be abandoned in the child with the immature teratoma as the portal vein and the superior mesenteric artery, the aorta and the IVC were all traversing the wall of the tumor.

Follow up ranged from 12 months to 108 months. Overall survival was 93.7%. The survival for children with malignant GCT was 100%. Median survival was 48 months. Event free survival was 80%. 1 child with an immature teratoma had abandonment of treatment as the tumor was unresectable and did not respond to chemotherapy. This child expired 11 months later.

Abdominal GCT

There were 7 children with intra-abdominal GCT. This constituted 6.5% of the study population. 3 of these were males and 4 were females. 3 had gastric teratomas, 1 had a teratoma anterior abdominal wall and 1 had a teratoma of the liver and 2 had intra-abdominal teratoma.

Table 11: Distribution of Abdominal GCT According Site

Site	Gastric	Abdominal Wall	Liver	Intra-abdominal
Number	3	1	1	2

5 (72%) of these children presented with mass abdomen. 1 (14%) child had an exomphalos, and 1 (14%) child had pain abdomen.

On radiological screening the size of the tumor ranged from 6cm to 15 cm in greatest dimension.

6 of these children underwent laparotomy and excision of these tumors. 4 of these lesions were diagnosed to be benign on biopsy. 1 child had an immature teratoma of the lesser curve of the stomach. 1 child had a needle biopsy, which showed malignant histology. The child had neoadjuvant JEB chemotherapy.

Table 12: Distribution of Abdominal GCT according to Histology

Histology	Malignant	Benign	Immature Teratoma
Number	1	4	2

One child with the malignant tumor had elevated AFP levels which did not decrease with chemotherapy. The child underwent 2 cycles of chemotherapy after which her treatment was abandoned. She eventually died within a few days.

One child with an immature teratoma also underwent preoperative chemotherapy and excision of tumor.

Follow up ranged from 15-120 months. 6 of the 7 children survived making the overall survival 85.8%. Median survival was 42 months. Event free survival was 80%. 1 child had abandonment of treatment and died 2 months later. 1 child had a gastro-esophageal reflux which was treated by medical measures.

Mediastinal GCT

5 children had thoracic teratomas constituting 4.7% of the study population. The age of these children at diagnosis ranged from 3 years to 14 years. Median age was 11 years. 4 (80%) were girls and 1(20%) was a boy.

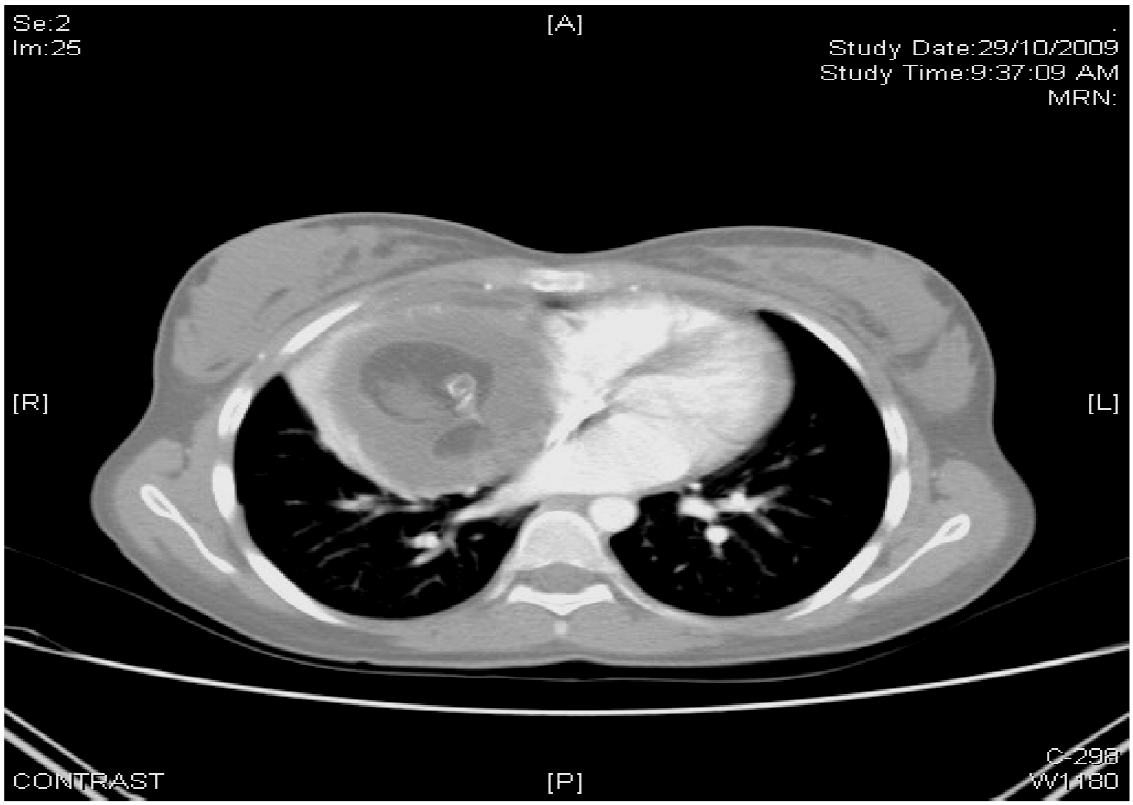
These children presented with varied symptoms. 1 had pain in the right chest, 1 had respiratory distress, 1 had fever and loss of appetite, and 1 child had hemoptysis.

Table 13: Distribution of Symptoms in Thoracic GCT

Symptom	Pain Chest	Respiratory Distress	Fever and Loss of appetite	Hemoptysis
Number	1	1	1	1

Radiological screening revealed 4 of these masses to be located in the anterior mediastinum, and 1 extending to the thoracic aorta from the thymus. The masses ranged from 7.5 cm to 12 cm in greatest diameter.

Figure 27: CT scan of a Child with Mediastinal GCT



The tumor markers were normal in all these children. Operative approach was through a thoracotomy and excision of the tumor in 4 children. 1 child had a median sternotomy. The operative findings showed large tumors containing hair, cheesy material in all these tumors. In one child the tumor was extending to the thoracic aorta.

Biopsy was consistent with mature teratoma in all these children. All of these children survived the treatment. Median survival was 54 months. One child has concomitant factor VII deficiency.

Thoracoabdominal GCT

One child was diagnosed with a thoracoabdominal teratoma. He was a male and 12 months at the time of diagnosis.

He presented with breathing difficult. X-ray showed a radiopaque mass in the right hemithorax. Due to the breathing difficulty and mass a CT was done which showed a 12 cm by 10 cm heterogenous mass in the posterior mediastinum which was extending into the abdomen.

To relieve him of his symptoms a right thoracotomy and excision of the thoracic part of the mass was done. Biopsy revealed a yolk sac tumor. He was given 2 cycles of JEB chemotherapy which was followed by laparotomy and excision of abdominal part of the mass.

4 cycles of chemotherapy was given post operatively. He is alive and well. His growth is adequate for age. He has been on follow up for 24 months.

GCT at Miscellaneous Sites

6 children had tumors at miscellaneous sites constituting 5.6% of this study population. 5(83%) of these were female and 1 (17%) was male. Age ranged from 2 months to 13 years.

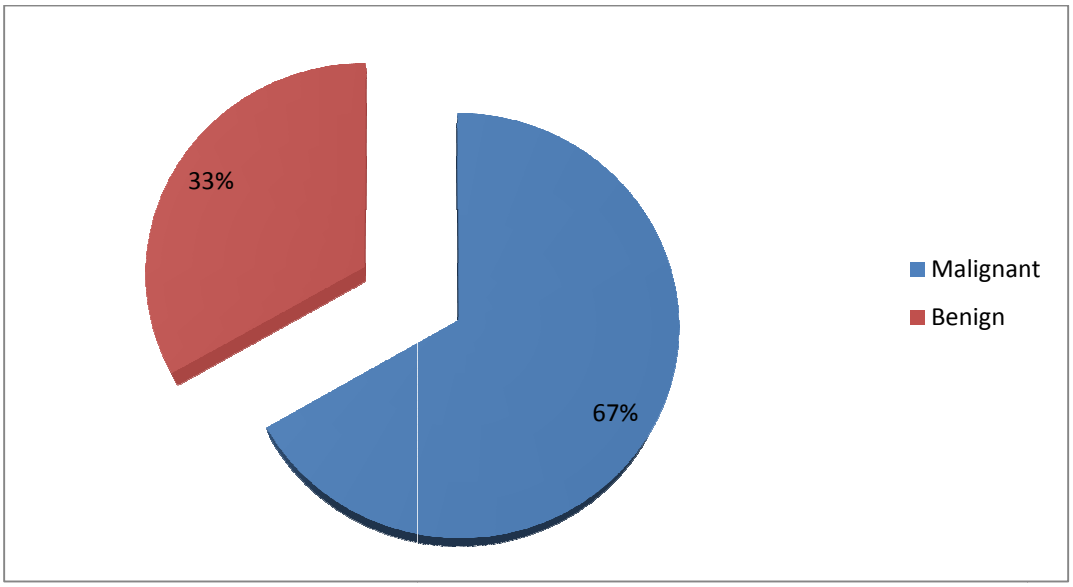
These children had varied presentations. 2 children presented with a mass on the right side of the neck.1 of these children had an associated mass right thigh. 2 children presented with bleeding per vagina at 7 months and 10months of age. 1 child had a mass in the right gluteal region with an associated hypospadias. 1 child presented with chest pain.

Table 14: Site of miscellaneous tumors

Site	Neck	Vagina	Gluteal	Lung
Number	2	2	1	1

The AFP was raised in 4 children ranging from 2410 IU/ml to 58000 IU/ml. All 4 were diagnosed to have malignant germ cell tumors. The size of the tumors of the neck ranged from 10cm to 20 cm in greatest diameter. The gluteal mass was 3 cm and the vaginal mass ranged from 3cm to 4 cm in greatest dimension.

Figure 28: Distribution according to histology in Miscellaneous Site GCT

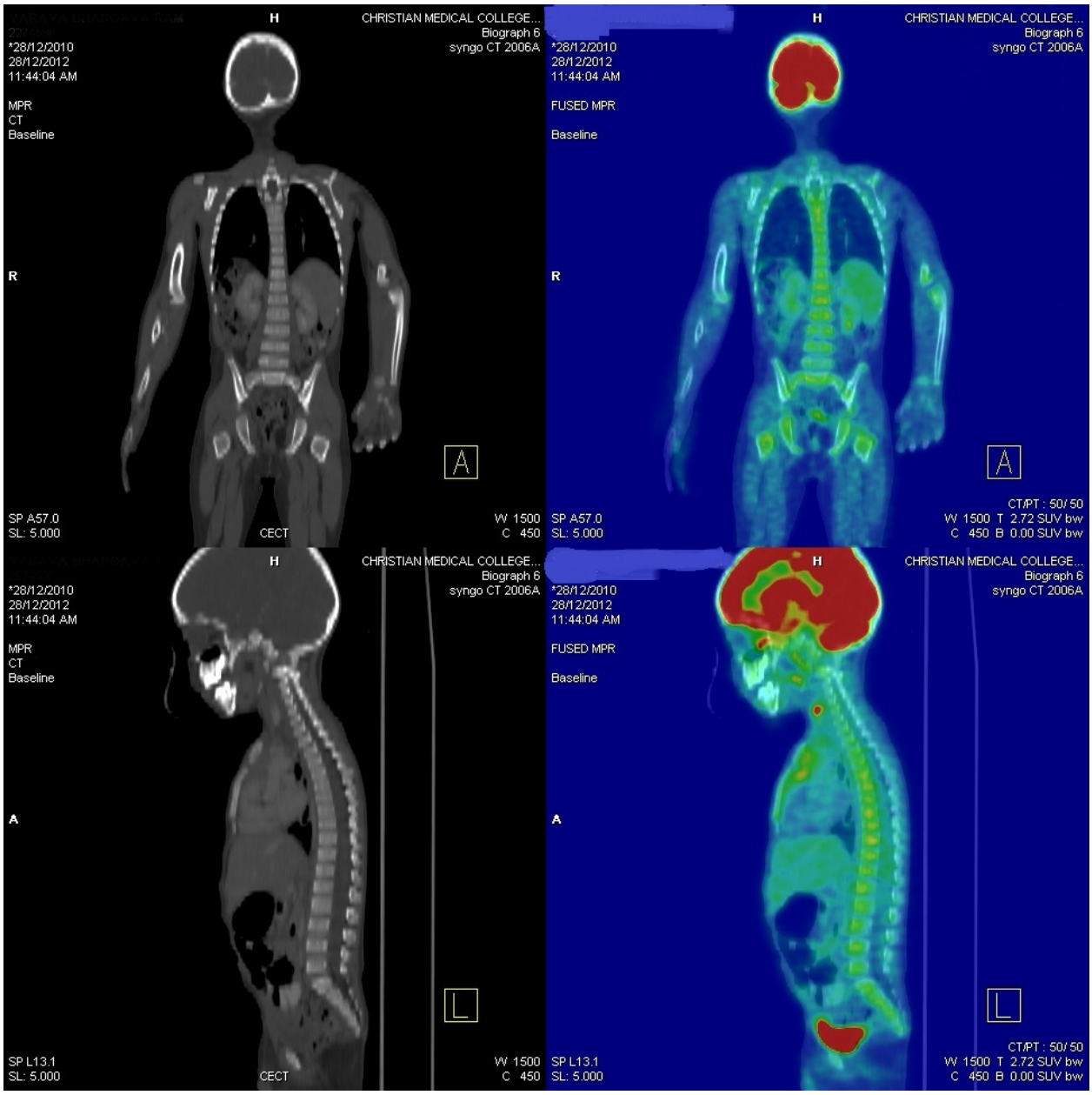


3 of these children were given neoadjuvant chemotherapy. 1 of these was a child with malignant neck GCT and one a vaginal GCT and 1 with lung GCT. 3 children had no chemotherapy but primary excision of the mass.

Follow up ranged from 12-120 months. The child with the metastatic germ cell tumor had abandonment of treatment. 5 children survived. The overall survival was 80%. Median survival was 71 months. The event free survival also is 80%. The child with the gluteal teratoma had right lower limb weakness and is on physiotherapy.

Figure 29: X-ray of an Infant with Cervical GCT

Figure 30: PET CT in a Child with Malignant Testicular GCT showing no residual disease



Discussion

Extracranial Germ cell tumors (GCTs) are rare tumors which occur in children and adolescents. We found an incidence of 0.1% among all paediatric malignancy seen in CMC Vellore and 8-10% of all Paediatric solid tumors treated here. Rescorla reported an incidence of 1-3% of childhood tumors, Khanna et al and Sarin and Bhatnagar in their review, reported an incidence of 7-10% among solid tumors in childhood.[1,2,5–8]

These tumors are commonly seen in females. Our study had a similar findings with 64% tumors diagnosed in female children with a female to male ratio of 1.8:1. A higher incidence among females has been reported in literature.[1,2,6,7]

Tumors were almost equally distributed among 0-1year, 1-5 years, 5-10years, and 10-16 years with distribution being 27%, 29%, 21% and 23% respectively. Some series have reported a bimodal peak for age groups while others have reported a different age peak for different sites. [1,2,6,7]

Gonadal GCTs formed the largest group in our study with 44% (n=47) distribution. The ovary was the commonest site involved with 28% (n=30) children forming this group. This contrasts earlier series by Billmire and Grosfeld[3], and Isaacs[6], Abubakar et al[22] which have reported sacrococcygeal teratomas to be the commonest. However some series have shown gonadal GCTs to predominate [7,39,47]. Some series report a higher incidence of non gonadal GCTs in early childhood and predominance of gonadal GCTs during adolescence [12,49,50].

Benign GCTs formed a majority in our series with 54% (n=58) being mature or immature teratomas. 46% (n=49) were malignant. Khanna et al reported a 34.1% incidence of malignancy, Sarin and Bhatnagar 13-17%, Schropp et al 21%, and Billmire and Grosfeld 28%. [3,7,8,51]

Imaging and tumor markers were used to diagnose GCTs. The tumor markers were elevated in all malignant GCTs and in infants with benign teratomas. Tumor markers returned to normal levels once surgery was undertaken or chemotherapy was started. Tumor markers showed an increase in case of recurrence. A decrease in tumor markers was not seen in case the tumor did not respond. Imaging in the form of ultrasound scan, CT scan, MRI and Pet were used to evaluate patients for diagnosis and response to treatment. CT scan and MRI were used in case of recurrence. Tumors which responded to neoadjuvant chemotherapy had a significant decrease in size and the reverse was true for tumors which did not respond. PET CT was used to delineate any residual disease or new foci of disease following completion of therapy. Several reports have emphasized the usefulness of imaging techniques and tumor markers in GCTs which are intrapelvic, abdominal, retroperitoneal and intrathoracic. [1,10,13,22,35,44,46,48,52,53]

Chemotherapy in the form of Carboplatin, Etoposide and Bleomycin (JEB), or Cisplatinum, Etoposide and Bleomycin (PEB) were used to treat patients with malignant GCTs. Several series have shown very good outcomes for GCTs especially of the gonads.[1,4,8,19,46,49,54]

Neoadjuvant chemotherapy was used in malignant ovarian GCTs based on tumor markers and imaging only. Response was seen by decrease in size of tumors and levels of tumor markers on follow up investigation. Following 2-4 cycles of chemotherapy, surgery was performed. This was followed by 2-4 cycles of JEB or PEB chemotherapy. Preoperative chemotherapy has been used in the MAKEI and MAHO protocols (5). Other series suggest upfront surgery followed by

chemotherapy for most extracranial malignant GCTs(33). Some series have reported usage of both preoperative and postoperative chemotherapy for malignant GCTs[20].

Chemotherapy was also used in some children with immature teratomas in our series. Earlier studies propagated the use of chemotherapy for all children with immature teratomas citing a high chance of recurrence. This was based on treatment protocols which are still followed in adults[55]. Earlier series have reported treatment with a combination of chemotherapy and radiotherapy in combination with surgery(56).Most studies now combine a complete excision followed by close follow up of all patients with immature teratoma[1,2,19,47].

Radiotherapy has been used to treat the local area in non seminomatous germ cell tumors. This modality has not been used in our series.[4,35,46]

The overall survival (OS) for all GCTs in our series was 95%. The median survival was 50 months; 51 months among females and 44 months among males. The median survival for children with benign GCTs was 58 months for immature teratomas was 48 months and for malignant GCTs was 44 months (p=0.020). The overall survival in malignant GCTs was 85.2%. Most studies reviewed by us mention an OS of 70-95% for malignant GCTs depending on stage and site of disease. The low stage gonadal tumors have an excellent overall survival of 90-100%.[1,8,18,19,25,35,44,49]

The event free survival (EFS) in all GCTs in our study was 85%. The EFS in females was 85% and in males was 84%. The EFS for all malignant GCTs was 75.9%, for immature teratomas was 87.4% and for benign tumors was 100%. There are different reports in literature which place EFS at 63-95% in malignant GCTs. EFS varies for different sites. This will be discussed in the individual tumor sites.[18,35,46,52]

Testicular tumors were present in 17% (n=17) patients in our series. This is the third largest group in our series. 64% (11/17), patients were below 5 years of age and malignancy was present in 76.5% (n=13) patients. Testicular GCTs were present in 10% of patients in the series report by Billmire and Grosfeld[3], 17% by Brodeur et al[35], as the third commonest by Khanna et al[7] and 27% by Wollner et al(9) and 18% by Gobel et al[5]. Wang et al reported a 33.3% incidence of malignancy[31], 100% by Khanna et al, and 22%-63% in other studies[1]. Most authors talk about benign tumors predominating during early childhood and malignant tumors in adolescence[1,2,4].

OS and EFS were 85% and 71% respectively. Most studies now report a 100% survival for stage I and II (30,57,58), and 93% for all stages[39].

26.4% (n=30) children presented with ovarian GCTs with 60% (n=18) of the tumors having malignancy and 10% (n=3) presenting as acute abdomen with torsion. This was the largest group in our study. Ovarian GCTs have been found to be the commonest site with varied incidence of malignancy in several reports by Brodeur et al reporting ovarian tumors as 30% of their study[35], 26% by Gobel et al[5], and 50% by Wollner et al. The ovary as the second most common site for GCTs has been seen in studies by Billmire et al[18], Khanna et al [7], and by Suita et al[39]. A high incidence of malignancy in our study can be explained by CMC Vellore being a tertiary level institution and where the patients are referred for advanced management.

The methods for diagnosis were imaging by way of USG scans, CT and MRI. Tumor markers in addition were used to substantiate the diagnosis. These methods are now commonly adopted for diagnosis of GCTs in literature.[3,5,13,16,18,46,47]

83% (n=15) of the children with malignant ovarian GCTs were treated on the basis of imaging and tumor markers without biopsy, using neoadjuvant chemotherapy followed by surgery and

adjuvant chemotherapy. This protocol has been followed by the MAKEI and MAHO studies[5] and also in the UKCCSG GCII trials [49] and has been mentioned by Sarin and Bhatnagar[8]. The POG, CCG groups follow upfront surgery for either complete resection, staging and debulking followed by chemotherapy[3,16,18,33,46,54,59].

The OS and EFS for malignant ovarian GCT was 90% and 85% respectively. Median survival was 44 months. With the newer protocols followed OS and EFS are in the range of 83%-95% and 93-95% respectively as reported in several studies for malignant ovarian GCT[4,5,16,18,47,59].

1 of the subjects is married after completion of treatment for malignant ovarian GCT. She is the mother of 2 children. There are reports in literature of fertility after treatment for gonadal GCTs.[34]

23% (n=25) patients in this series had Sacrococcygeal teratomas (SCT). 72% (n=18) were female and 28% (n=7) were male with a male to female ratio of 1:2.8. 16%(n=4) presented at birth, 32% (n=8) presented before 1 year of age and 48%(n=12) presented after 1 year of age. SCT is the most common tumor in most series reported in literature with comprising 50% of tumors of the series[1,3,5,6,60].

40% (n=10) of SCT were Altman type 1. The incidence of malignancy in Altman Type II to type IV tumors increased exponentially with type IV having 100% malignant components. This is comparable to reports by Billmire[1], Ashour and Ehlalaby [14]Altman[21], and Abubaker et al[22].

The diagnosis and management were according to protocol. 1 child with malignant components on needle biopsy received neoadjuvant chemotherapy. All children with malignant components received chemotherapy following resection. OS and EFS in malignant SCT was 80% and 60% respectively. Recurrence was seen in 7 (28%) patients with SCT. A similar OS and EFS has been

reported in literature[1,3,5,6,19,23]. High recurrence rate of 20-55% has been reported in a study by De Backer et al[61].

Retroperitoneal GCTs comprise 16% (n=16) of our study group. 8 were females and 8 were males. 68.8% (n=11) were benign. Retroperitoneal GCTs comprise 4-5% of case series reported in literature, and a majority are benign[3,5].The diagnosis and management were according to protocol. 1 child with immature teratoma underwent a laparotomy to resect the tumor which had to be abandoned as the tumor was unresectable. 2 cycles of JEB chemotherapy was tried and the child did not respond. The OS and the EFS for malignant tumors was 100% and 80% respectively. Similar reports are available in literature. [3,5,35]

Abdominal GCTs comprised 6.5% (n=7) of our study population. 57% (4) were female and 43%(n=3) were male. 1 of these tumors was malignant. 1 child with immature teratoma on biopsy was given neoadjuvant chemotherapy following which she underwent resection. The protocol followed for immature teratoma has been reported earlier[56]. Some protocols follow the complete resection and close follow up of these tumors[1,5]. The OS and EFS were 85.8% and 80% respectively. Most series report similar incidence[1,5]

Mediastinal tumors comprised 4.7% (n=5) of our study population. 80% (n=4) were females and all these tumors were benign. Treatment given was primary resection of these tumors. Most series report mediastinal tumors as being mostly benign with a small proportion being malignant[1,5]. Among mediastinal GCTs 86% are reported to be benign by Billmire et al[45], and 43% by Moran and Suster[37].

70% of children with tumors of miscellaneous sites had malignancy. These included the neck, the lung, genitals and the bladder. A majority of these were females. Diagnosis was based on

imaging, tumor markers and biopsy. Chemotherapy was given in 4 children. OS and EFS was 80% in malignant GCTs of miscellaneous sites. Reports of similar findings and treatment are found in literature[1,2,7,62]. One child with vaginal Yolk Sac tumor was given only chemotherapy and this child is well on a 4 year follow up.

Conclusions:

Germ cell tumors are rare set of tumors. These occur at many sites. They can be benign in the form a mature teratoma, immature teratomas or malignant from the seminomas to the embryonal carcinoma.

The commonest Germ cell tumors are the Sacrococcygeal teratomas, although in our series ovarian germ cell tumors were more common (28% against 23%).

Germ cell tumors occur more commonly in females (64% in our series).

There is a variable age range from infancy to adolescence. Most occur in early childhood. (56% were between 0 to 5 years in our series).

Benign tumors predominate (54% in our series).

Malignant tumors are diagnosed by tumor markers imaging and biopsy. Treatment for malignant tumors is multimodality with neoadjuvant chemotherapy, surgery and adjuvant chemotherapy.

Chemotherapy using JEB (Carboplatin, Etoposide and Bleomycin) is highly effective in down staging disease and decreasing the size of tumors thus making surgery easier.

Neoadjuvant chemotherapy without biopsy can be used to treat malignant ovarian GCTs as this helps in reducing tumor burden and shrinking the tumor.

Long term survival is possible in malignant germ cell tumors after the introduction of Cisplatinum based chemotherapy.

Recurrence is a possibility in cases of immature teratomas or malignant germ cell tumors where therapy is not complete.

Chemotherapy can be tried in high grade immature teratomas but response is variable.

There are a few sequelae of treatment like infertility, ovarian failure, neurogenic bowel and bladder and interstitial lung disease which should be kept in mind while treating such patients.

Long term follow up for sequelae of treatment and recurrence is advisable in patients who have immature teratomas or malignant disease.

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Appendix

Annexure-1- Information Letter

From

Department Of Paediatric Surgery

CMC Vellore

Dear……..,

Greetings from Christian Medial College Vellore.

We have looked at your record and found that you have been treated for Germ Cell Tumor at CMC Vellore.

At present we are undertaking a project to study these tumors in all children who have suffered from similar tumors.

We would like to have a check up for you in the Paediatric Surgery OPD. along with some blood investigations and an X-ray of the chest. This would tell us how you are doing.

Please do make an appointment for paediatric surgery OPD on any day from Monday to Saturday and request the MRO to contact Dr Deepak S Singh.

We would be obliged if you could consider this as most important.

This would help us in screening you for any problems and help us in treating patients who suffer from a similar tumor.

If for some reason you are unable to come please do let us know by letter how you are doing.

Thanking You

Yours Sincerely

Dr Deepak Samson Singh

Mob:+91 8940318971

Annexure-2 Information sheet and consent Form

Christian Medical College, Vellore

Department of Paediatric Surgery

Clinical Profile of Children With Extracranial Germ Cell Tumors.

Information sheet

You/your child are invited to be part of a study to improve the current knowledge about your disease condition. This study will help other children who later come to hospital with the same complaints. By agreeing to be a part of this study, you will contribute to recognizing early how severe the disease is and thereby starting appropriate treatment immediately. The severity of your disease and the final treatment received will be compared to the information collected from you in the beginning.

The information collected from you will include

1. History – This includes details regarding your general health and the illness which you have been treated for
2. Clinical examination – Includes evaluation by the attending doctor on admission to the hospital
3. Investigations – Includes the results of relevant blood and urine tests, radiological investigations, and biopsy reports.
4. Details of treatment- includes surgery performed, chemotherapy given and post treatment follow up

Whether you/your child accept or decline to be a part of this study will not affect your further treatment at this hospital

The benefits of joining in this study will be that the treating doctor will gain a better understanding of your disease and its process thereby help in improving treatment protocols for the same. We will also be conducting a blood test and a chest x-ray, free of cost, which is part of regular follow up.

There is no disadvantage or complication that can happen to you/your child by participating in this study as this study does not interfere in the treatment provided by the care taker.

All details including personal data, assessment of the doctor during and after the operation will be kept confidential.

We aim to include about 76 people from this hospital in this study who have been diagnosed to have this illness in the last 10 years.

Participation in this study is purely voluntary, and you can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which you are otherwise entitled.

In case of doubts/ questions, please contact Dr. Deepak Samson Singh, Dept Of Paediatric Surgery, CMCH Vellore. Ph no: +918940318971

Informed Parental Consent form to Participate in a clinical trial

Christian Medical College, Vellore

Department of Paediatric Surgery

Clinical Profile of Children With Extracranial Germ Cell Tumors

Study Number:

Subject's Initials: _____ Subject's Name: _____

Date of Birth / Age:_____

Please initial box

(i) I confirm that I have read/been read to and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my child's participation in the study is voluntary and that I am

free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:_____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature of the Witness: _____

Date:_____/_____/_____

Name of the Witness: _____

Annexure-3 Proforma

A Clinical Profile of Children With Extra Cranial Germ Cell Tumors

Hosp No: **STUDY No:**

DEMOGRAPHY

Name: Gender: Date Of Birth:

Address:

Mobile Telephone:

Patient education status:

Date of First visit:

Other Visits

Current Status: Alive and well

Alive but with complications

Alive in remission

Died- if yes cause of death: Complication of disease, complication of chemotherapy, Complication of surgery

Abandonment Of Treatment

Co-morbidities:

Other associated anomalies/ Diseases

OPERATIVE FINDINGS :

Type of Surgery: laparoscopic /Open Date of surgery:

Size Of mass: Site of Mass: Findings:

Post op Complications: (Infection / Mortality)

CLINICAL ASSESSMENT							
Weight **Kg**							
Height/Length **Cm**							
Mass							
Abdominal distention							
Respiratory symptoms							
Loss of weight							
Loss of apetite							
Bleeding PV							
Mass- site							
Mass- size							

Laboratory ASSESSMENT							
Hemoglobin/ PCV							
Total Counts							
Differential Counts							
AFP							
Beta HCG							
LDH							
Creatinine							
Electrolytes							
Ultrasound							
Site Of Mass							
Size of The mass							
CT Scan							
Site Of mass							
Size Of mass							
MRI							
POST Chemo and							

surgery imaging							
Biopsy							
Beningn							
Malignant							
elements							
Bone							
cartilage							
Muscle							
Neural							
teeth							
others							

Preoperative Chemotherapy

Admission						
Chemotherapy						
Agents						

Post Op Chemotherapy

Admission						
Chemotherapy						
Agents						

Outcomes

Survival

Disease Free:

Recurrence:

Site of Recurrence:

Abandonment Of Treatment

Late Complication:

Growth

Respiratory

Renal

Death:

Cause Of death: Complication of disease, Complication Of Surgery, Complication Of Chemotherapy

Duration of Follow up

Master Chart

S No	HNUM	Gender	Age	Age	code	Pathology	Biopsy	DIAGNOSIS	Biopsy no
1	328914C	2	6	6mths	1	1	Malignant yolk sac tumor	Yolk Sac tumor Right Testis	20232/03
2	427610c	2	12	1yr	1	1	Malignant Germ cell Yolk sac tumor, infiltrating skin	yolk sac tumor right testis	3610/04
3	598476C	2	156	13yrs	1	1	Metastatic Non seminomatous GCT	NS GCT, Metastatic	28863/05
4	673815C	2	24	2yrs	1	1	Endodermal Sinus Tumor	Endodermal Sinus Tumor Right Testis-metastatic	18053/05
5	099477D	2	12	1yr	1	3	Teratoma with focal low grade immaturity	? Teratoma left testis mature	27204/07
6	056218D	2	36	3yrs	1	1	Yolk sac tumor	Yolk Sac Tumor Left Testis	18997/07
7	218169D	2	168	14yrs	1	2	mature cystic teratoma right scrotum	Mature cystic Teratoma Left Testis	11111/08
8	338781D	2	156	13yrs	1	2	mature cystic teratoma left scrotum	Mature teratoma left testis	2361/09
9	475827D	2	12	1yr	1	2	Bilateral mature teratomas	Bilateral testicular teratomas	19243/09
10	573940D	2	48	4yrs	1	1	Yolk Sac tumor right testis	Non Seminomatous GCT -malignant	35517/09
11	461571D	2	36	3yrs	1	1	Malignant Germ cell Yolk sac tumor, infiltrating skin	Recurrent Testicular GCT disemanated	ABD
12	498834D	2	48	4yrs	1	1	Yolk sac tumor	Yolk Sac Tumor left testis	22545/09
13	720167D	2	96	8yrs	1	1	yolk sac tumor	Yolk Sac Tumor Right Testis	19954/10
14	765911D	2	156	13yrs	1	1	embryonal carcinoma lymphovascular invasion	GCT- embryonal carcinoma right testis	28013/10
15	131119F	2	168	14yrs	1	1	mixed GCT with embryonal,yolk sac elemants, immature teratoma	GCT- right testis with retroperitoneal lymph nodes	4032/12
16	155544F	2	36	3yrs	1	1	yolk sac tumor	GCT- yols\k sac tumor left testis	9567/12
17	446196C	2	48	4yrs	1	1	necrotic tumor probably GCT	Yolk Sac tumor tesis- undescended testis	9085/04
18	275668C	1	144	12yrs	2	2	benign cystic teratoma	benign teratoma ovary	
19	500061c	1	120	10yrs	2	1	mixed GCT ovary	Mixed GCT ovary	16951/04
20	500041c	1	96	8yrs	2	2	mature teratoma right ovary	mature cystic teratoma right ovary	18020/04
21	533791C	1	132	11yrs	2	3	Immature Teratoma Grade II	(R) ovarian cyst ? malignant cystic teratoma	25643/04
22	550245C	1	144	12yrs	2	2	mature teratoma right ovary	Right ovarian cyst - ? teratoma	27967/04
23	737128C	1	96	8yrs	2	2	mature teratoma left ovary	Mature Cystic Teratoma Right Ovary	31407/05
24	702818A	1	144	12yrs	2	1	mature teratomas with extensive hyalinization	Malignant teratoma ovary	709/06
25	804372C	1	144	12yrs	2	1	dygerminoma right ovary	Right Ovarian Dysgerminoma	11550/06
26	759358C	1	132	11yrs	2	1	mature teratoma right ovary	Malignant GCT Ovary	10553/06
27	132772D	1	48	4yrs	2	2	mature cystic teratoma left ovary	Mass per abdomen ? teratoma (L) ovary	32664/07
28	905136c	1	180	15yrs	2	1	post chemo with scanty viable tumor	malignant GCT left ovary	9595/07
29	041839D	1	84	7yrs	2	1	yolk sac tumor right ovary	Yolk sac tumor right ovary	16484/07
30	108030D	1	72	6yrs	2	2	mature cystic teratoma left ovary	Mature teratoma left ovary	28388/07
31	952629C	1	132	11yrs	2	1	malignant mixed GCT, yolk sac 70%, dysgerminoma 30%	Malignant Mixed GCT right ovary	2995/08
32	511844D	1	96	8yrs	2	1	benign cystic teratoma	(R) ovarian mass (cystic teratoma)	26070/09
33	323734D	1	156	13yrs	2	1	dygerminoma	Dysgerminoma right ovary	30031/08
34	884765B	1	108	9yrs	2	2	mature cystic teratoma right ovary	Mature Teratoma Right Ovary	7596/10
35	715542D	1	144	12yrs	2	2	mature cystic teratoma right ovary	Mature Cystic teratoma Right Ovary	20745/10
36	714822D	1	84	7yrs	2	1	tumor with mature elements post chemo	GCT malignant right ovary	31038/10
37	025340F	1	48	4yrs	2	2	mature cystic teratoma right ovary	(R) ovarian mass ? teratoma	29385/11
38	039126F	1	144	12yrs	2	1	no residual tumor post chemo	GCT- malignant right ovarian	1955/12
39	067044F	1	72	6yrs	2	3	high grade immature teratoma	GCT- high grade immature teratoma ovary	35128/11
40	236942F	1	168	14yrs	2	1	no residual tumor post chemo	ovarian teratoma, malignant	33992/12
41	356203f	1	84	7yrs	2	1	dysgerminoma+ yolk sac /no residual tumor post chemo	Mixed GCT dysgerminoma and yolk sac tumor ovary	41129/12

42	895521C	1	60	5yrs	2	1	no residual tumor post chemo	Ovarin GCT-right	17375/12
43	138014F	1	72	6yrs	2	1	dysgerminoma left ovary	Ovarian GCT Left-dysgerminoma	7220/12
44	796161D	1	84	7yrs	2	1	noresidual tumor/ yolk sac and embryonal elements	Left ovarian malignant GCT	30982/11
45	225912F	1	84	7yrs	2	1	nil viable tumor	GCT Ovary	33081/12
46	746398c	1	60	5yrs	2	1	dysgerminoma	Malignant GCT Right Ovary	365/751/06
47	793022c	1	144	12years	2	1	malignant mixed GCT pred YST, EC, Focal teratomatous	Mixed GCT right ovary	10753/06
48	262524F	1	30	2.5yrs	3	1	malignant neoplasm/ residual mature teratoma post chemo	Sacrococcygeal Teratoma-malignant	11104(a)
49	109013F	2	120	10yrs	3	1	poorly diff malig neo-yolk sac or embryonal ca/myxopapillary ependymoma	Malignant Presacral Embryonal Carcinoma Status POST CHEMO	2256/12
50	221069F	1	12	1yrs	3	2	mature teratoma	Neurogenic bladder ,Status opeated case of sacrococcygeal teratoma (SCT) ,Recurrent urinary tract infection	PS2
51	227459F	2	12	1yrs	3	1	no residual tumor in the presacral mas, liver biopsy germ cell tumor	RECURRENT METASTATIC PRESACRAL TERATOMA in liver	21645/12
52	919403D	2	24	2yrs	3	1	teratoma with focal yolk sac/ post chemo focalyolk sac component	Sacrococcygeal teratoma with yolk sac tumor	23046/11
53	675137D	1	2	2mths	3	2	mature teratoma	Sacrococcygeal teratoma	11435/10
54	515866D	1	36	3yrs	3	2	mature teratoma	Sacrococcygeal teratoma	28882/09
55	454699D	1	12	1yrs	3	1	malignanat GCT yolk sac tumor/ no viable tumor post chemo	Malignant presacral GCT (yolk sac tumour) (presacral teratoma)	14703/09,31
56	561376D	1	12	1yrs	3	2	mature cystic teratoma	Sacrococcygeal teratoma	35163/09
57	381557D	1	1day	1day	3	2	mature cystic teratoma	Ruptured sacrococcygeal teratoma	259/09
58	173089D	1	24	2yrs	3	2	mature cystic teratoma	Sacrococcygeal teratoma	4406/08
59	943889C	1	1day	1day	3	3	immature teratoma GIII	SCT Immature GIII	36619/06
60	936427C	1	8	8mth	3	1	malignant neoplasm/ residual mature teratoma post chemo	Presacral GCT Malignant	33661/06510
61	644385C	1	8	8mths	3	3	immature Teratoma	Sacrococcygeal Teartoma immature)	18835/06
62	855437C	1	84	7yrs	3	2	mature teratoma	presacral Teratoma Benign	20763/06
63	768568C	2	84	7yrs	3	2	maturet teratoma	Sacro coccygeal teratoma	3324/06
64	814878C	2	12	1yrs	3	2	mature cystic teratoma	Sacrococcygeal teratoma	12836/06
65	641470C	1	84	7yrs	3	2	mature cystic teratoma	Recurrent sacrococcygeal teratoma	13482/06
66	743163C	2	4	3.5mth	3	2	mature teratoma	Sacrococcygeal teratoma	31754/05
67	739333C	1	1day	1day	3	2	mature cytic teratoma	Sacro coccygeal teratoma	32017/05
68	467911C	1	1day	1day	3	2	mature cytic teratoma	Post op case of sacrococcygeal teratoma excision ,Admitted for CIC	13423/04
69	662165C	1	30	2.5yrs	3	2	mature cystic teratoma	Presacral teratoma Altman type III	17941/05
70	687998C	1	24	2yrs	3	1	malignant gct/no evidence of tumor	Malignant GCT Sacrococcygeal	20785/05
71	947770D	2	108	9yrs	3	2	benign cystic teratoma	Excised sacrococcygeal teratoma with neuro vascular weakness of rectal sphinct	
72	765226C	1	42	3.5yrs	3	1	malignant gct/mature teratoma	Malignant Sacrococcygeal Teratoma	2262/06/118
73	612325C	1	36	3yrs	4	2	mature teratoma	Retroperitoneal teratoma	7492/05
74	698034C	2	96	8yrs	4	2	mature teratoma	Retroperitoneal teratoma	23063/05
75	886746C	2	16	1.4yr	4	2	Germ cell tumor consistent with endodermal sinus tumor/ no viable tumor post chemo	Endodermal Sinus Tumor retroperitoneum	25391/06/95
76	009007D	1	24	2yrs	4	2	mature teratoma	Retroperitoneal teratoma (pancreato duodenal region)	10530/07
77	366976D	1	14	1.2yrs	4	2	monodermal teratoma	Retroperitoneal Monodermal Teratoma	38704/08
78	456626D	2	168	14yrs	4	2	mature teratoma	Pseudo pancreatic cyst ,Status excision cystic teratoma tail of pancreas	16106/09
79	579839D	2	36	3yrs	4	1	yolk sac tumor	Retroperitoneal malignant germ cell tumor metastatic to liver	37285/09
80	716077D	1	6	6mths	4	2	mature teratoma	(L) retro peritoneal teratoma	20534/10
81	839820D	2	30	2.5yrs	4	2	mature teratoma	Mature teratoma pelvic mass (Retroperitoneal	41543/10
82	852197D	1	60	5yrs	4	1	yolk sac tumor/no viable tumor cells	Yolk Sac Tumor right suprarenal region	425/11/1166
83	072986F	1	5	5mths	4	3	immature teratoma	GCT- high grade teratoma right suprarenal	38338/11
84	305472f	1	11	11mths	4	2	mature teratoma	Inter aortocaval Teratoma- mature	35035/12

85	572546D	2	18	1.5yrs	4	1	yolk sac tumor	Yolk Sac tumor Left renal Mass	36579/09
86	192542D	2	36	3yrs	4	2	mature teratoma	Mature Cystic teartoma Head of pancreas	5738/08
87	144400D	2	7	7mths	4	2	mature teratoma	Mature Teratoma Retroperitoneum	36899/07
88	075729F	1	6	6mths	4	3	immature teratoma grade III	Immature teratoma retroperitoneum	37528/11
89	890450D	1	18	1.5yrs	5	2	mature teratoma	INTRA ABDOMINAL TERATOMA	6316/11
90	288697F	2	156	13yrs	5	3	immature tetratoma containing skin bone hair cartilage and glial tissue	Mature teratoma lesser curve of stomach	33835/12
91	653168D	1	3	2months	5	3	immature teratoma	Gastric teratoma attached to lesser curve of stomach-malignant	8411/10
92	223485C	2	36	3yrs	5	2	mature teratoma	Subacute intestinal obstruction status exomphalos major with benign cystic mature teratoma anterior abdominal wall excision	PS1
93	349659C	2	24	2yrs	5	2	mature teratoma	Post op case of benign gastric teratoma with GER	PS
94	545899C	1	8	8mths	5	2	Mature cystic teratoma	Benign Cystic Teratoma Liver	27722/04
95	2396659f	1	168	14years	5	1	Mixed GCT	Malignant GCT abdomen	9455a
96	123496f	2	12	1yrs	6	1	Yolk Sac Tumor	Thoracoabdominal yolk sac tumor	14786/12/30
97	566973D	1	168	14yrs	7	2	mature teratoma	Mature teratoma mediastinum	36158/09
98	252261D	1	120	10yrs	7	2	mature teratoma	Mature Cystic Teartoma Thymus	17858/08
99	155237D	1	36	3yrs	7	2	mature teratoma	Anterior mediastinal teratoma	912/08
100	663388C	1	144	12yrs	7	2	mature cystic teratoma	Thymic teratoma ,Mild factor VII deficiency	16913/05
101	073376F	2	132	11yrs	7	2	mature teratoma	MEDIASTINAL TERATOMA	38637/11
102	440337C	1	72	6yrs	8	2	mature teratoma	Rt. cervial teratoma (biospy report awaited)	8206/04
103	380874D	1	10	10mths	8	1	Malignant yolk sac tumor	Yolk Sac tumor Vagina and Cervix	40301/08
104	696260D	1	7	7mths	8	1	Yolk Sac Tumor	GCT Vagina malignant	
105	914933D	1	3	2.5mths	8	1	metastatic germ cell tumor right thigh	GCT- metastatic GCT from neck	10221/11
106	760859C	2	24	2yrs	8	2	benign cystic teratoma	Benign Cystic Teratoma Left Gluteal	10409/09
107	696221C	1	136	13yrs	8	1	yolk sac tumor/no residual tumor	Malignant GCT Upper lobe left lung	

	B HCG	**follow up**	**preop chemo**	**Chemo**	**follow up chemo**	**Survival**	**recurrence**	**follow up chem**	**follow up mnths**	**Status**	**FFUD**	**LFUD**	**Follow up problems**
	<1			1		yes	yes	yes	60	1	2003	Sep-08	1
	<1			1		yes	yes		36	1	Feb-04	Jun-07	1
	<1			1,3	IVAD	no		no	12	2	Feb-05	Mar-06	2
	<1			1,3	no	yes	no	yes	24	1	Jul-05	Jan-07	1
	<1			2		yes	no	yes		1	Sep-07	Oct-13	1
0.8	<1			1,3	no	yes	no	yes	60	1	Aug-07	13-Dec	3
	<1			2		yes	no		48	1	Apr-08	Dec-13	1
	<1			2		yes	no	yes	48	1	Sep-09	Dec-13	1
	<1			2		yes	no	yes	48	1	Jun-09	Dec-13	1
	<1			1,3		yes	no	yes	36	1	Nov-09	Dec-13	1
				2		ABD	yes			2	May-09	May-09	2
	<1			1,3		yes	no	yes	36	1	Jul-09	Sep-09	4
	<1			1,3		yes	no	yes	36	1	Apr-10	Dec-13	1
	<1			1,3		yes	no	yes	36	1	Aug-10	Dec-13	1
	28240	2.82		1,3	VeIP6cycles	yes	no	yes	12	1	May-12	Dec-13	1
	<0.1			1,3		yes	no	yes	12	1	Mar-12	Dec-13	1
	8.83			1,3		yes	no	yes	56	1	Apr-04	Dec-08	1

				2		yes	no	yes	120	1	Apr-03	Dec-13	1
	<1			2		yes	no		108	1	Apr-04	Dec-07	1
	<1			2		yes	no	yes	108	1	Apr-04	Dec-13	1
	<1			2		yes	no	yes	0	1	Oct-04		4
				2		yes	no	yes	108	1	Nov-04	Dec-13	1
	<1			2		yes	no	yes	96	1	Jun-05	Dec-13	1
	<1		yes 4	1,3		yes	no	yes	84	1	Jan-06	Dec-13	1
	196900	14900/154/4.72		1,4		yes	no	yes	84	1	Apr-06	Dec-06	4
	93000	<0.1	yes3	1,3		yes	no	yes	84	1	Jan-06	Dec-13	3
	<1			2		yes	no	yes	60	1	Nov-07	Dec-13	1
	<1		yes 6	1,3		yes	no	yes	72	1	Oct-05	Dec-13	1
	<1			1,3		yes	no	yes	72	1	Jun-07	Dec-13	1
	<1			2		yes	no	yes	72	1	Sep-07	Dec-13	1
	<1			1		ABD	NA		nil	2	Jan-07	Dec-08	4
	<1			2		yes	no	yes	48	1	Aug-07	Dec-13	1
	27.8	<0.1		1,4		yes	no	yes	48	1	Jan-08	Dec-13	1
	<1			2		yes	no	yes	36	1	Jun-10	Dec-13	1
	<1			2		yes	no	yes	36	1	Jun-10	Dec-13	1
1.68	21840	508/35.5/0.3	yes 4	1,3		yes	no	yes	36	1	Jun-10	Dec-13	1
	<.01			2		yes	no	yes	24	1	Sep-11	Dec-13	1
	1207	0.867<0.1	yes4	1,3		yes	no	yes	24	1	Nov-11	Dec-13	1
	<0.1	2.2		1,3		yes	no	yes	24	1	Nov-11	Dec-13	3
0.1	212.8	<0.1	yes 4	1,3		yes	no	yes	18	1	Jun-12	Dec-13	1
	48.1	<0.1	yes 3	1,3		yes	no	yes	12	1	Nov-12	Dec-13	1
	223.19	<0.1	yes 2	1,3		yes	no	yes	17	1	Sep-12	Dec-13	3
	<0.1			1,3		yes	no	yes	18	1	Feb-12	Dec-13	1
	1076	0.37	yes4	1,3	VeCP	yes	yes	ABD	12	2	Oct-10	Oct-11	4
	28.68	<1	1	3		1	2		12	1	Sep-12	Dec-13	1
		<1	yes6	1.3		yes	yes	yes	36	1	Jan-06	Dec-08	1
	44.1	<1	no	1,3		yes	no	yes	70	1	Apr-06	Dec-11	1
0.76	0.1		yes4	1,3		1	2	yes	16	1	Aug-12	Dec-13	1
	<0.1		yes 12	1,4		1	yes	yes	20	1	Feb-12	Dec-13	1
	<0.1			2		1	no		36	1	Oct-10	Dec-13	3
5.9	<0.1		yes4	1,3		1	yes	yes	18	1	Jun-12	Dec-13	1
	0.165		yes 4	1,3		ABD/ died may 2012	Yes	yes	12	2	Jul-11	May-12	2
	<1.0		no	2		yes	no	yes	36	1	Apr-10	Dec-13	1
				2		yes	no	yes	48	1	Sep-09	Dec-13	1
1.2	<1		yes 4	1,3		yes but died of sepsis in Apr 2013	no	yes	48	2	Sep-09	Apr-13	2
	<1			2		yes	no	yes	48	1	Oct-09	Dec-13	1
	25.5			2		1	2	yes	48	1	Jan-09	Dec-13	1
	<1			2		1	2	yes	60	1	Feb-08	Dec-13	1
	<1		no	1,3		yes	yes after 5 years	yes	72	1	Dec-06	Dec-13	1
1.3	<1		yes4	1,3		yes	yes after 7mths	yes	84	1	Nov-06	Dec-13	1

	<1			2		yes	2	yes	84	1	Jan-06	Dec-10	1
	<1			2		yes	no	yes	72	1	Jul-06	Dec-13	1
	<1			2		1	2	yes	84	1	Feb-06	Dec-10	1
	<1			2		1	2	yes	84	1	May-06	Dec-13	1
	<1			2		yes	excised at 12 days of birth, recurred	yes	84	1	May-05	Dec-08	3
	<1			2		1	2	yes	96	1	Dec-05	Dec-10	1
0.9	4.51	0.65	no	2		yes	no	yes	96	1	Dec-05	Dec-13	1
				2		yes	2	yes	96	1	Apr-05	Dec-10	3
	<1			2		yes	no	yes	96	1	Jul-05	Dec-10	1
	<1		yes5	1,3		yes	2		96	1	Jun-05	Dec-08	1
				2		1	2	yes	120	1	Sep-11	Dec-13	1
	<1		yes4	1,3		yes	no	yes	84	1	Jan-06	Dec-09	1
	,1			2		1	2	yes	96	1	Mar-05	Dec-13	1
	<1			2		1	2	yes	96	1	Sep-05	Dec-07	1
	7.41		yes	1,3		1	yes	yes	12	1	Sep-06	Dec-07	4
	<1			2		1	2		72	1	Apr-04	Dec-13	1
	<1			2		1	2		60	1	Dec-08	Dec-13	1
	<1			2		1	2	yes	48	1	May-09	Dec-13	1
	<1		yes	1,4		1	2			1	Nov-09		4
	<1			2		1	2		36	1	Jun-10	Dec-13	1
	<1			2		1	2	yes	36	1	Dec-10	Dec-13	1
2.7	<1		yes4	1,3		1	2	yes	24	1	Jan-11	Dec-13	1
	<0.1		yes 4	1,3		1	2	yes	24	1	Dec-11	Feb-12	2
	<0.1			2		1	2	yes	12	1	Oct-12	Dec-13	1
0.947	1.5		yes6	1,3		1	2	yes	36	1	Nov-09	Dec-13	1
	<1			2		1	2	yes	60	1	Feb-08	Dec-13	1
	<1			2		1	2	yes	72	1	Dec-07	Dec-09	1
	<0.1		no	1,3		ABD	na	yes	11	2	Nov-11	Oct-12	2
	<1			2		1	2	1	32	1	Feb-11	Dec-13	1
	<0.1			2		1	2	1	15	1	Oct-12	Dec-13	1
4.6	<0.1		2	1,3		1	2	1	48	1	Dec-09	Dec-13	1
	<1		2	2		1	2	1	120	1	Nov-04	Dec-13	1
	<1		2	2		1	2	1	120	1	Aug-05	Dec-08	1
	<1			2		1	2	1	108	1	Nov-04	Dec-08	1
	73.39	38.8	yes2	1,3	no	ABD				2	Jul-12		2
6.6	0.1		1	1,3		1	2	1	24	1	Jan-12	Dec-13	1
	<1		2	2		1	2	1	48	1	Oct-09	Dec-13	1
	1		2	2		1	2	1	60	1	Jun-08	Dec-12	1
	<1		2	2		1	2	1	60	1	Jan-08	Dec-13	1
	<1		2	2		1	2	1	96	1	Jul-05	Dec-13	1
	<0.1		2	2		1	2	1	25	1	Dec-11	Dec-13	1
	<1			2		1	2	1	118	1	Apr-04	Dec-10	1
	<1			2		1	2			1	Dec-08		2

<1	1	1,3	1	2			1	May-10	Dec-13	1
<1	1	1,3	2		ABD		2	Mar-11	Apr-11	2
	2	2	yes	no	1	57	1	Jan-08	Dec-13	1
<1	yes4	1,3	1	2	1	96	1	Sep-05	Dec-13	1

Presentation	**size**	**site**	**Complication of chemo**	**Hb**	**creat**	**USG/CT**
right scrotal swelling	10x10	right scrotum	nil	12		no mets
mass abdomen and generalized lymphadenopathy	10x5x5	epigastrium	nephrotic symdrome	10.6	0.5	10x5x5
mass right scrotum		right testis	nil	12.2	0.5	normal
mass left scrotum	2x3	extra testicular	nil	13		normal
mass left scrotum	4x3	left testis	asthma	10.9	0.5	right parailiac lymphnodes
mass right scrotum	6x8	right testis	nil	13		multiple cysts in right hemiscrotum testis normal
mass left scrotum		extra testicular	nil	13		extratesticular mass
bilateral scrotal mass	4x4,5x4	both testis	nil	11	0.4	bilateral testicular cystic lesions
right scrotal swelling	4x4	right testis	nil	10.1		right hemiscrotal soft tissue masse
right scrotal swelling	3x5	right testis		9.9	0.5	mass right scrotum
left scrotal swelling	3x4	left testis	nil	10	0.5	confluent pre and paraaortic LNE
right scrotal swelling	3x2	right testis	nil	9.9	0.6	confluent paraaortic nodes
right scrotal swelling	6x6	right testis	nil	13	0.8	heterogenous right testis
right testicular tumor	5x6cm	right testis	nil	10.8	0.6	confluent necrotic mass from renal hilum to bifurcation of aorta
left scrotal swelling	5cm	left testis	nil	11.1	0.6	no evidence of intrabdominal mets
vomiting and pain	5cm	right undescended testis	nil	10	0.4	6x6 cm retroperitoneal mass
abdominal mass	30x15	left ovary	nil	12	0.3	large retrperitoneal mass
abdominal mass	10x5	right ovary	nil	12	0.4	normal
abdominal mass	6x6x4	right ovary	nil	10	0.5	6.6x4.6x5.6cm mass - complicted cyst
abdominal mass, pain	9x6	right ovary	nil	10	0.7	7.3x5x4.5 cm mass in POD
pain abdomen, mass	8x4	left ovary	nil	14	0.7	left ovarian cyst
mass, ascitis	10x10	right ovary	nil	11.5	0.7	right ovarian cyst multiloculated compressing both ureters
mass	19x14	right ovary	nil	12	0.7	19x14x6cm mass right ovary
mass pain	15x7	right ovary	nil	10	0.6	15x7x6 cm tumor arising from pelvis, R HUN
mass.pain	7x5	left ovary	nil	11	0.5	8x7cm mass arising from left ovary
mass fever loss of wt pain		left ovary	nil	12	0.5	7.9x4.9x9.5 mass pelvis left ovary
mass pain	7x10	right ovary	nil	10	0.4	7x8x10cm mass right adenexa
pain abdomen		left ovary	nil	10		3x4x3 cm left ovary
pain abdomen	13x14	right ovary		8.2	0.5	13x3x14 pelvic mass
pain and vomiting	10x6	right ovary	nil	11	0.6	10x7x5cm mass with calcification and fat
pain abdomen	10x10	right ovary	nil	10	0.6	10x14x10 cm heterogenous mass in pelvis
pain and vomiting	5x7cm	right ovary	nil	12	0.6	
pain and vomiting	7x5	right ovary	nil	12	0.6	7x4.9cm mass right ovary cystic
pain and vomiting and fever	9x13	right ovary	nil	8.8	0.6	9x15 mass right ovary

pain	4x3	right ovary	nil	12	0.5	4.6x3.5 cm mass right ovary
pain and mass	20x15	right ovary	nil	10	0.7	15x12x10cm mass in pelvis with central necrosis and right HDN,
pain and mass	5x5	right ovary	nil	11	0.7	5x5cm mass right ovary
mass ,distention fever	22x16	right ovary	nil	7.6	0.6	16x22 cm complex cyst arising from pelvis
mass	11x9	right ovary	nil	10	0.6	11x9 cm mass right ovary
pain and mass	10x7	right ovary	nil	13	0.5	10x7x5cm mass right ovary, 2 other lesions posterior to it
pain	7x7	left ovary	nil	11	0.5	5x7 mass left ovary
mass	5x5	left ovary	nil	10	0.4	11x10cm mass arising from left ovary
pain abdomen	12x10	right ovary	nil	13.4	0.4	normal
mass	7x8	right ovary	nil	12	0.6	mass right adenexa
mass	7x6	right ovary	nil	11	0.7	mass right ovary
mass	5x4.5	presacral	nil	8.8	0.4	presacral mass with superficial component, no liver mets
pain	3.8x1.4	presacral	nil	12	0.7	presacral mass38x14 mm
mass	10x12	sacrococygeal	nil	12	0.5	nil
mass	5x3	presacral	nil	8.8	0.5	recurrent mass presacral regio with lung and liver mets
mass right gluteal region and paraparesis	10x12	right gluteal region	nil	9.1	0.4	10x12cm presacral mass
mass sacrococygeal	7x5	sacrococygeal	nil	12	0.4	
mass sacrococcygeal	6x4	sacrococygeal	nil	11		6.3x4.4x7.6cm mass in sacrocosccygealregion with minimal presacral
mass sacrococcygeal	3x3cm	sacrococygeal	nil	10	0.4	7x 7 cm mass extending to L4 and below the coccyx lung mets
sct mass	3x3cm	sacrococygeal	nil	12	0.4	5x9x4 cm mass extending from L5 S1 level to perineum
sct mass	10x10	sacrococygeal	nil	17	0.4	
sct mass	20x20cm	sacrococygeal	nil	12	0.5	14x8x10 cm mass with large presacral component and external compo perineum
sct mass	10x7	sacrococygeal	nil	14	0.4	10x7 cm mass with minimal intrapelvic extension
sct mass operated at 12 days of life recurred	4x4	sacrococygeal	nil	11.5	0.6	1.7x2.6x1.5cm mass anterior to rectum
sct mass	3x2	sacrococygeal	nil	12		2x1cm mass
sct mass	5x4.5	sacrococygeal	nil	12	0.6	5.2x4.3x5.4 cm mass in the presacral area
sct mass	3x3cm	sacrococygeal	nil	13		4x3 cm mass presacral region
sct mass	5x4	sacrococygeal	nil	13	0.4	1.9x2x2.9cm lesion in sacrococcygeal region
mass with discharge from multiple sinuses	5x15x20	sacrococygeal	nil	12	0.5	16x11x7cm mass in intergluteal cleft with cystic areas
mass in the sct with	15x15	sacrococygeal	nil	9	0.5	9.5x5.7 cm mass in sacral region
mass sct	5x7	sacrococygeal	nil	20	0.6	
mass sct	10x12	sacrococygeal	nil	14	0.4	15x10 cm mass extending from aortic bifurcation to perineum
mass sct	4x2	sacrococygeal	nil			13x8.7x8 cm mass from pelvis to the ischium
mass sct sudden increase in size	8x8x6	sacrococygeal	nil	9.9	0.4	10x5x7 cm mass which is predominantly presacral
mass sct	10x12	sacrococygeal	nil	13	0.6	
mass sct biopsied outside	5x15x20	sacrococygeal	nil	9.6	0.4	5.1x4.5x3.4cm mass in the perineum with intrapelvic extension and di
mass distention abdomen	left hypochondrium	retroperitoneum				
mass distention abdomen	8x4x2cm	lesser sac	nil	13	0.6	mass in the lesser sac measuring
mass distention abdomen paraparesis	15x9x9.4cm	retroperitoneum extending to thorax	nil	8.9	0.4	mass retroperitoneum 15x9x9.4cm extending into thorax, extending in
mass and distention of abdomen	15x10	lesser sac	nil	12		15x10x8 cm mass in lesser sac
mass and distention of abdomen	15x12	retroperitoneum	nil	11.9	0.4	12x8.9cm multiloculated cyst compressing kidney and causing hDN
mass and distention of abdomen	11x10	tail of pancreas	nil	13	0.6	11x10x8 cm mass in the region of tail of pancreaas
pain and distention fever	multtiple	retroperitoneum mets in liver	niil	12	0.7	multiple large confluent masses 13x12x8.5cm

mass left abdomen	15x15	retroperitoneum	nil	12	0.5	10x8cm mass in the left retroperitoneum with solid and cystic compon
left abdominal mass	10x10	retroperitoneum	nil	12	0.6	12x9x13cm mass occupying the abdomen and pelvis with left HUN
pain and distentionand vomiting	14x10	right suprarenal region	nil	12	0.4	14x10x9.5cm mass in the right suprarenal region with central necrosis
abdominal mass	8x6	right suprarenal region	nil	11	0.4	8.3x6.1x8cm mass in the right suprarenal region
mass abdomen and UTI	10x10	interaortocaval	nil	14	0.3	10x10x8cm mass in the interaortocaval region from abdomen to pelvis
pain abdomen and mass	13x11	left kidney	nil	12	0.5	13x11cm mass arising in left kidney
abdominal pain	6x4	hepatoduodenal ligament	nil			6.9x4.1x4.5cm mass in the hepatoduodenal ligament
mass	10x12	left sided retroperitoneal tumor	nil	12	0.4	ascitis with septations and internal echoes
mass abdomen	6x10	right hypochondrium	non response to chemo	12	0.3	large intrabdominal lesion with septated cystic and echogenic areas
distention	5x5	retroperitoneal	nil	10	0.5	retroperitoneal teratoma
pain abdomen	8x7	anterior wall of stomach	nil	10.8	0.6	8x7 cm mass anterior to stomach and pancreas with calcification
mass	16x9x7	posterior wall of stomach	nil	10	0.4	large heterogenous mass in the upper abdomen
exomphalos	5x6	anterior abdominal wall	nil	10	0.5	mass abdominal wall
mass	5x7	anterior wall of stomach	nil	10	0.4	mass abdomen
mass and distention	16x10	liver	nil	10	0.4	cystic mass 10x9x9.5 exophytically arising from left lobe of liver
mass	occupying most of abdomen	abdomen	DiedJul2012			
breathing difficulty, abd distention	12x10	right thorax and abdomen	nil	11	0.4	Mass in the posterior mediatinum extending into abdome
pain right chest	7.3x7	anterior mediastinum	nil	14	0.6	mass in anterior mediastinum measurin 7.7x7.3 cm
loss of apetite, fever	8x8	mediastinum	nil	14	0.5	mass in the posterior mediastinum withattachment to thymus
abdominal pain	10x8	anterior mediastinum	nil	12.6	0.4	mass in anterior mediastinum measuring 12x10x8 cm
respiratory distress	8x5	anterior mediastinum	nil	12	0.4	mass 7.8x5.3 cm in anterior mediastinum
hemoptysis	4x5	anterior mediastinum	nil	14	0.5	mass attached to pericardium in left anterior mediastinum
mass right neck since birth	10x12	right side of neck	nil			
			nil			
bleeding pv	4x3	bladder and cervix	nil	12	0.4	mass occupying the vagina and the uterus
mass right neck, given bleo, affecte eye movement mass left thigh	20x20	neck		8	0.4	mass right neck
recurrent mass left gluteal region	3x3	left gluteal	nil	12	0.6	mass left gluteal region cystic
Fever and cough	Sep-05	left lung upper lobe	nil	11	0.6	15x13x9 cm mass occupying left thorax

op findings	**Biopsy**	**Ht**	**wt**	**Altman Type**	**Follow up ht**	**Follow up wt**
enlarged right testis	Malignant Germ cell Yolk sac tumor, infiltrating skin					
Mass abdomen	Metastatic Non seminomatous GCT					
enlarged tight testis	Endodermal Sinus Tumor	75	9.1			
enlarged left testis	Teratoma with focal low grade immaturity					
enlarged left testis	Yolk sac tumor	90	13.2		112	19.6
enlarge right testis	mature cystic teratoma right scrotum					
mass left testis	mature cystic teratoma left scrotum	120	30		176	45.9
enlarged bilateral testis	Bilateral mature teratomas					
enlarged right testis	Yolk Sac tumor right testis	108	17.2		116	20.2
enlarged right testis	Malignant Germ cell Yolk sac tumor, infiltrating skin		10			
enlargde left testis	Yolk sac tumor	99	13.2			

enlarged right testis	yolk sac tumor	125	19		141	27.9
enlarged right testis	embryonal carcinoma lymphovascular invasion	157	40.6		167	48.9
enlarged right testis	mixed GCT with embryonal,yolk sac elemants, immature teratoma	156	46		164	53.5
enlarged left testis	yolk sac tumor	96	14			
torted right testis with tumor in pelvis with adhesions	necrotic tumor probably GCT				118	20.3
large ovarian cyst 30x15cm	benign cystic teratoma					
large ovarian mass in right ovary	mixed GCT ovary					
8x8cm tumor right ovary	mature teratoma right ovary					
mass occupying most of abdomen						
9x6cm tumor right ovary	mature teratoma right ovary					
6x7 cm mass left ovary	mature teratoma left ovary	140	33		153	40.8
large ovarian mass in right ovary	mature teratomas with extensive hyalinization	156	38		168	55.5
19x14x6cm mass	dygerminoma right ovary	133	28			
large ovarian mass, ascitis	mature teratoma right ovary	146	30		164	70
twisted left ovarian mass	mature cystic teratoma left ovary					
10x8 cm left ovarian mass adherent to omentum	post chemo with scanty viable tumor	150	31.6			
10x8 cm right ovarian mass adherent to omentum	yolk sac tumor right ovary		14			
3x4x3 cm mass left ovary	mature cystic teratoma left ovary	135	20.8			
15x14cm mass right ovary	malignant mixed GCT, yolk sac 70%, dysgerminoma 30%	145	34			
10x8cm mass	benign cystic teratoma	143	25		155	33
10x10cm mass with torsion right ovary	dygerminoma	153	38		157	37
7x8cm torted ovary with gangrene of fallopian tube	mature cystic teratoma right ovary				139	30
7x5cm mass right ovary	mature cystic teratoma right ovary					
15x12x5cm right ovarian mass	tumor with mature elements post chemo	126	26		131	35
4x3 cm mass right ovary	mature cystic teratoma right ovary	126	26			
8x8x6cm mass right ovary	no residual tumor post chemo	149	30.6		150	32
5x4 cm mass right ovary	high grade immature teratoma					
10x8cm mass adherent to omentum	no residual tumor post chemo	150	40		151	36
5x3 cm mass with nodules in the retroperitoneum	dysgerminoma+ yolk sac /no residual tumor post chemo	125	20.7		126	20
2x1.5cm mass in the right ovary	no residual tumor post chemo	100	16		126	20
5x7 cm mass left ovary with torsion	dysgerminoma left ovary	125	25		126	35
5x5xm left ovarian mass	noresidual tumor/ yolk sac and embryonal elements	115	17		121	18
mass of right ovary adherent to sigmoid and deposits in the pelvic wall	nil viable tumor	103	13.9		102	13.2
7x8cm right	no viable tumor					
7x5cm mass right ovary	no viable tumor					
	mass in the presacral region	malignant neoplasm/ residual mature teratoma post chemo	82	III	8.8	93
	fibrosis in presacral region	poorly diff malig neo-yolk sac or embryonal ca/myxopapillary ependymoma	140	IV	28.2	144
	sacrococcygeal mass with bone and cartilage and hair	mature teratoma	88	I	12	100
no active residual disease although residual masses present	fibrosed mass in presacrum, mets in segment 5 and 6	no residual tumor in the presacral mas, liver biopsy germ cell tumor	89	IV	10.5	98
	large mass involving the presacrum 5x5 cm	teratoma with focal yolk sac/ post chemo focalyolk sac component	78	II	10.3	
	7x 5cm mass with minimal presacral extension	mature teratoma		I		
	7x5cm mass with minml presacral ext	mature teratoma		I		
no active residual disease although residual masses present	7x3 cm mass lefrt pelvic wall	malignanat GCT yolk sac tumor/ no viable tumor post chemo	84	III	10.6	100

	9x7 cm mass in the presacral region	mature cystic teratoma		III		
	10x10 cm mass with minimal presacral extension	mature cystic teratoma		I		
	large mass with presacral extension	mature cystic teratoma		II		
	SCT with minimal presacral ext, spillage of tumor into the wound/ residual mass in right parailiac regionand iliac nodes/ mass in the parailiac region and nodes		101	I	15	
no evidence of osseous mets	2x3x2cm mass anterior t sacrum	malignant neoplasm/ residual mature teratoma post chemo	67	III	9	104
	2x3 cm mass inferior to coccyx	immature Teratoma		I		
	5x4x5 cm large cyst and a 2x3 cm smaller cyst in the presacral area	mature teratoma		II		
	4x4 cm mass in the presacral area attached to coccyx	maturet teratoma		II		
	1.5x5cm mass in presacral area			II		
	15x15cm fleshy sacroccygeal mass containing cheesy material	mature cystic teratoma		I		
	10x7 cm mass in the sct	mature teratoma		I		
	5x7x5cm mass in the sacral region	mature cytic teratoma		I		
	large cystic mass in the sacral and presacral region	mature cytic teratoma		II		
	mass in the presacral region measuring 13x8x9 cm	mature cystic teratoma		III		
	mass with external componenet 4x3 cm densely adherent to posterior and right rectal wall and coccyx	malignant gct/no evidence of tumor	78	III	8	85
	mass in the sacrococygeal region	benign cystic teratoma		I		
	mass fixed to overlying skin and to coccyx	malignant gct/mature teratoma	91	II	10.5	108
well encapsulated mass behind left colon						
cystic lesion adherent to the head of pancreas.	mature teratoma					
hard mass adherent from T6-T8 infiltrating	Germ cell tumor consistent with endodermal sinus tumor/ no viable tumor post chemo				paraparesis	
mass in lesser sac in the pancreaticoduodenal region	mature teratoma					
large mass pushing sigmoid and descending colon medially	monodermal teratoma					
large cyst filled with debri with cartilage and hair, between transverse mesocolon and tail of pancreas	mature teratoma	161	36			
	yolk sac tumor					
15x15cm mass osterior to the left transverse colon	mature teratoma					
10x8 cm mass in the retroperitoneum extending from bladder to the left kidney	mature teratoma	69	7.7		75	8.9
7x6x8cm mass in the	yolk sac tumor/no viable tumor cells	50	11			
large cystic mass from the undersurface of liver to just above the pelvis	immature teratoma	63	5.5			
large retroperitoneal interaortocaval tumor from infradudenal ivc to the pelvis	mature teratoma	69	7.2		100	12
tumor arising from the upper pole of left kidney6x5x5cm	yolk sac tumor	75	10.4 2			
cystic mass head of pancreas	mature teratoma					
mass in the retroperitoneum left of the spine	mature teratoma					
large cystic mass adherent to liver splaying the right and left renal veins and IVC. Pushing duodenum and right kidney inferiorly	immature teratoma grade III		6.8			
		60	13		80	15
tumor adherent to liver arising from lesser curve of stomach	mature teratoma					
huge cystic tumor attached to the posterior wall of the stomach	immature tetratoma containing skin bone hair cartilage and glial tissue	60	3.1		82	9.8
large antreior abdominal wall defect with a mass containing hetrogenous cyst	mature teratoma	45	3		150	35
large mass attached to stomachwall	mature teratoma	40	3		101	16
15x8cm loculated tumor in the left lobe of liver		40	3		140	35
retroperitoneal tumor adherent to right lobe of liver extending to right thorax through a diaphragmatic defect	yolk sac tumor/ no residual tumor post chemo	76	7.7		87	9.6
2 cyts interconnected containing hair and soft tissue	mature teratoma	135	35		150	55
8x8 cm mass anterior to thoracic aorta attached to thymus	mature teratoma	135	32		150	45

15x10cm mass in anterior mediastinum collapse of lung	mature teratoma	120	25	134	30
4x5cm mass in the anterior mediastinum attached left lung and pericardium	mature cystic teratoma	135	35	150	50
5x5 cm mass arisinf from left lat aspect of thymus with cheesy materieal and fine hair	mature teratoma	163	41	167	45
10x12 cm cyst adherent to right cheek intraoral and sternomasroid	mature teratoma				
		67	6.7	78	11.4
nil	metastatic germ cell tumor right thigh				
3x3 cm cystic mass containing bone and hair	benign cystic teratoma	86.5	11.4		
Mass upper lobe of left lung	yolk sac tumor/no residual tumor	146	39	151	58

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March 11, 2013

Dr. Deepak Samson Singh
PG Senior Registrar
Department of Paediatric Surgery
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Sub: **FLUID Research grant project NEW PROPOSAL:**
Clinical Profile of Children with Extra Cranial Germ Cell Tumors.
Dr. Deepak Samson Singh, PG Senior Registrar, Paediatric Surgery, Dr. Sampath Karl, Dr. John Mathai, Paediatric Surgery, Dr. Leni G Mathew, Dr. Rikki Rorima John, Child Health I, Dr. Sridhar Gibikote, Radiology, Dr. Ramani M Kumar, Pathology.

Ref: IRB Min. No. 8168 dated 09.01.2013

Dear Dr. Deepak Samson Singh,

I enclose the following documents:-

1. Institutional Review Board approval
2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes.

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr Nihal Thomas
MBBS MD MNAMS DNB (Endo) FRACP(Endo) FRCP(Edin)
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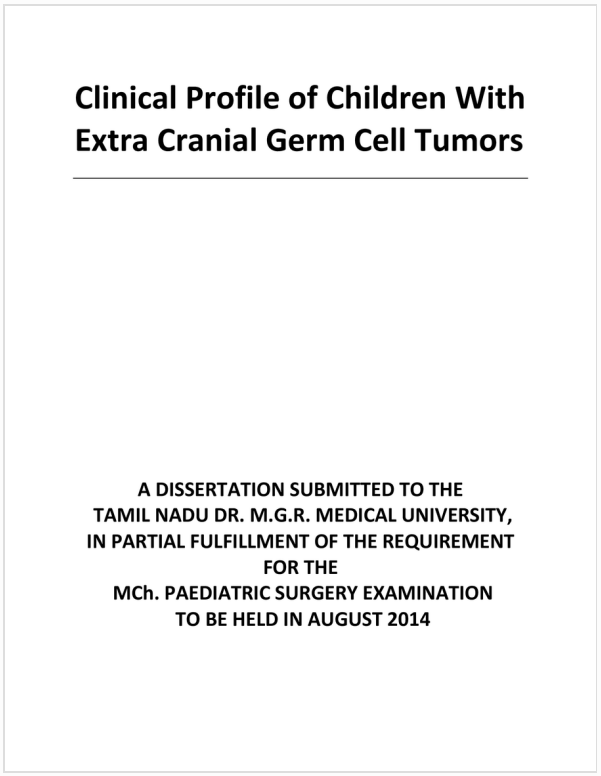

Clinical Profile of Children With Extra Cranial Germ Cell Tumors

A DISSERTATION SUBMITTED TO THE
TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY,
IN PARTIAL FULFILLMENT OF THE REQUIREMENT
FOR THE
MCh. PAEDIATRIC SURGERY EXAMINATION
TO BE HELD IN AUGUST 2014

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